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IN ENGLISH TRANSLATION



CONSULTANTS BUREAU, INC.

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by K. B. Yatsimirskii and V. P. Vasil'ev

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CONTENTS

	PAGE	RUSS. PAGE
Investigation of the Equilibrium of Three Liquid Phases in Three-Component Systems. I. <u>N. I. Nikurashina, R. V. Mertslin and I. D. Gos'kova</u>	3127	3161
Investigation of the Equilibrium of Three Liquid Phases in Three-Component Systems. II. <u>N. I. Nikurashina, R. V. Mertslin, A. B. Gagarina and G. L. Kozlova</u>	3133	3167
Field of Three Liquid Phases in a Four-Component System. <u>R. V. Mertslin and K. I. Mochalov</u>	3138	3172
Systems With a Lower Ternary Critical Point. I. Layer Formation in the Chloral Hydrate- Water-Pyramidon System. <u>E. F. Zhuravlev</u>	3144	3178
Ternary Reciprocal System of Sodium and Potassium Acetates and Caproates. <u>E. I. Pochtakova</u>	3149	3183
Physicochemical Study of Systems with Diphenylamine. I. <u>V. V. Udovenko and K. P. Topornina</u>	3155	3189
Synthesis and Reactions of Vinyl Ethers of Silanols. <u>S. I. Sadykh-Zade and A. D. Petrov</u> ...	3159	3194
Interaction of Isopropylolithium with Esters. <u>A. D. Petrov, Kao Chin-lang and E. I. Alipova</u> .	3164	3199
Stereochemistry of Nitrogen Heterocycles. IV. Stereoisomerism of 2-Methyl-4-hydroxy- decahydroquinoline. <u>D. V. Sokolov, G. S. Litvinenko and K. I. Khudneva</u>	3169	3204
Investigation in the Field of 2,1,3-Thiadiazole Chemistry. X. Synthesis and Investigation of Derivatives of Pyrimidine-2,1,3-thiadiazole. <u>V. G. Pesin, A. M. Khaletskii and L. V. Zolotova-Zolotukhina</u>	3178	3214
Some Heterocyclic β -Chloroethylamines. <u>G. I. Braz, V. P. Bronovitskaya and K. N. Kurdyumova</u>	3182	3219
Synthesis of Compounds of the 1-Alkylthiobuten-1-yne-3 Type. <u>I. I. Guseinov, E. N. Prilezhaeva and M. F. Shostakovskii</u>	3186	3223
Mechanism of the Reaction Between Thiols and 1-Alkylthiobutenynes and Some Properties of Bis-Alkylthiobutadienes. <u>E. N. Prilezhaeva, I. I. Guseinov, B. V. Lopatin and M. F. Shostakovskii</u>	3190	3227
Cyclopropanes and Cyclobutanes. VI. <u>p-Nitrophenyl- and p-Aminophenylcyclopropanes. R. Ya. Levina, Yu. S. Shabarov and V. K. Potapov</u>	3196	3233
δ -Lactones. XVIII. Interaction of 5,6-Dialkyl- α -pyrones with Acetylenedicarboxylic Ester. New Synthesis of 3,4-Dialkylphthalic Acids. <u>N. P. Shusherina, R. Ya. Levina and V. M. Shostakovskii</u>	3200	3237
Chemistry of Selenophene. XX. Condensation of Selenophene-2-aldehyde with Esters of Substituted Acetic Acids and Nitromethane. <u>Yu. K. Yur'ev, N. N. Mezentsova and V. E. Vas'kovskii</u>	3203	3239

CONTENTS (continued)

	PAGE	RUSS. PAGE
Catalytic Alkylation of Benzene and Toluene with Propyl Alcohols. <u>M. B. Turova-Polyak, N. V. Rudenko and I. L. Parbuzina</u>	3207	3243
Absorption Spectra of Disubstituted Benzenes with Similarly Directing Functional Groups. II. Absorption Spectra of Nitrobenzaldehydes. <u>A. E. Lutsii and V. T. Alekseeva</u>	3211	3248
Unsaturated Hydrocarbons. VIII. Synthesis and Some Conversions of 3-Phenylheptadien-4,6-di-3. <u>I. L. Kotlyarevskii, M. I. Bardamova and M. S. Shvartsberg</u>	3215	3252
Unsaturated Hydrocarbons. IX. Contribution on the Aromatization of Aryl Substituted Compounds. <u>M. S. Shvartsberg and I. L. Kotlyarevskii</u>	3218	3255
Investigation in the Field of Hydroxy Derivatives of Anthracene. VI. Reactivity of Nitrosoanthrols and Nitrosoanthrolsulfonic Acids. <u>M. V. Gorelik and S. V. Bogdanov</u>	3222	3258
Thermal Decomposition of Esters of N-Substituted,7-Aminomethyl-6-(8-hydroxyethyl)-1-azabicyclo-(3,2,1)-octane. <u>V. Ya. Furshtatova, E. E. Mikhlin and M. V. Rubtsov</u>	3227	3263
Synthesis of Py-N-alkyltetrahydroharmine. <u>M. V. Rubtsov, L. N. Yakhontov and D. M. Krasnokutskaya</u>	3232	3268
N-Derivatives of 2,6-dimethylpiperidine <u>E. S. Nikit-skaya, V. S. Usovskaya and M. V. Rubtsov</u>	3236	3272
Addition of Full Esters of Phosphorous and Phosphinous Acids to Conjugated Systems. VIII. Interaction of Ethylphosphinous Esters with Acrylic and Methacrylic Acids. <u>V. A. Kukhtin and L. A. Khismatullina</u>	3240	3276
Interaction of Potassium Acetate with β -Chloroketones. Addition of Carboxylic Acids to Vinyl Ketones. <u>Yu. A. Arbuzov and Yu. P. Volkov</u>	3242	3279
The Field of Organic Insectofungicides. XLV. Synthesis of Alkyl Aryl Chlorothiophosphates and Alkyl Aryl Thiophosphamides. <u>N. N. Mel'nikov, Ya. A. Mandel'baum, Z. M. Bakanova and P. G. Zaks</u>	3249	3286
The Field of Organic Insectofungicides. XLVI. Synthesis of Some Phosphonoacetic Acid Derivatives. <u>N. N. Mel'nikov, Ya. A. Mandel'baum and V. I. Lomakina</u>	3252	3289
The Field of Organic Insectofungicides. XLVII. Interaction of Aryldiazonium Salts with Dialkyl Dithiophosphates. <u>N. N. Mel'nikov, A. F. Grapov and K. D. Shvetsova-Shilovskaya</u>	3255	3291
Radical and Ionic Alkylation of the Aromatic Nucleus. VIII. A Contribution on Trichloromethylation of Naphthalene. <u>I. P. Tsukervanik, M. B. Gorovits and G. K. Makarichev</u>	3259	3295
Amino Ketones of the 4-Quinazolone Series as Analogs of Febrifugine. II. Derivatives of Methyl Alkyl Ketones. <u>Lu Yü-hua and O. Yu. Magidson</u>	3263	3299
Heterocyclic Compounds. 61. Synthetic Anesthetics. XXXI. Synthesis of Esters of the β -Form of 1-Alkenyl-4,5-dimethyl-4-piperidols. <u>I. N. Nazarov, A. Sh. Sharifkanov and K. F. Danilova</u>	3269	3305
Heterocyclic Compounds. 62. Synthesis of 1-Alkenyl-2,4,5-trimethyl-4-piperidols. <u>I. N. Nazarov, A. Sh. Sharifkanov and K. F. Danilova</u>	3274	3310
Mechanism of the Conversion of Vinylethynylcarbinols into Vinylisocoumarans. <u>I. N. Nazarov, G. P. Verkholetova and I. V. Torgov</u>	3277	3313

CONTENTS (continued)

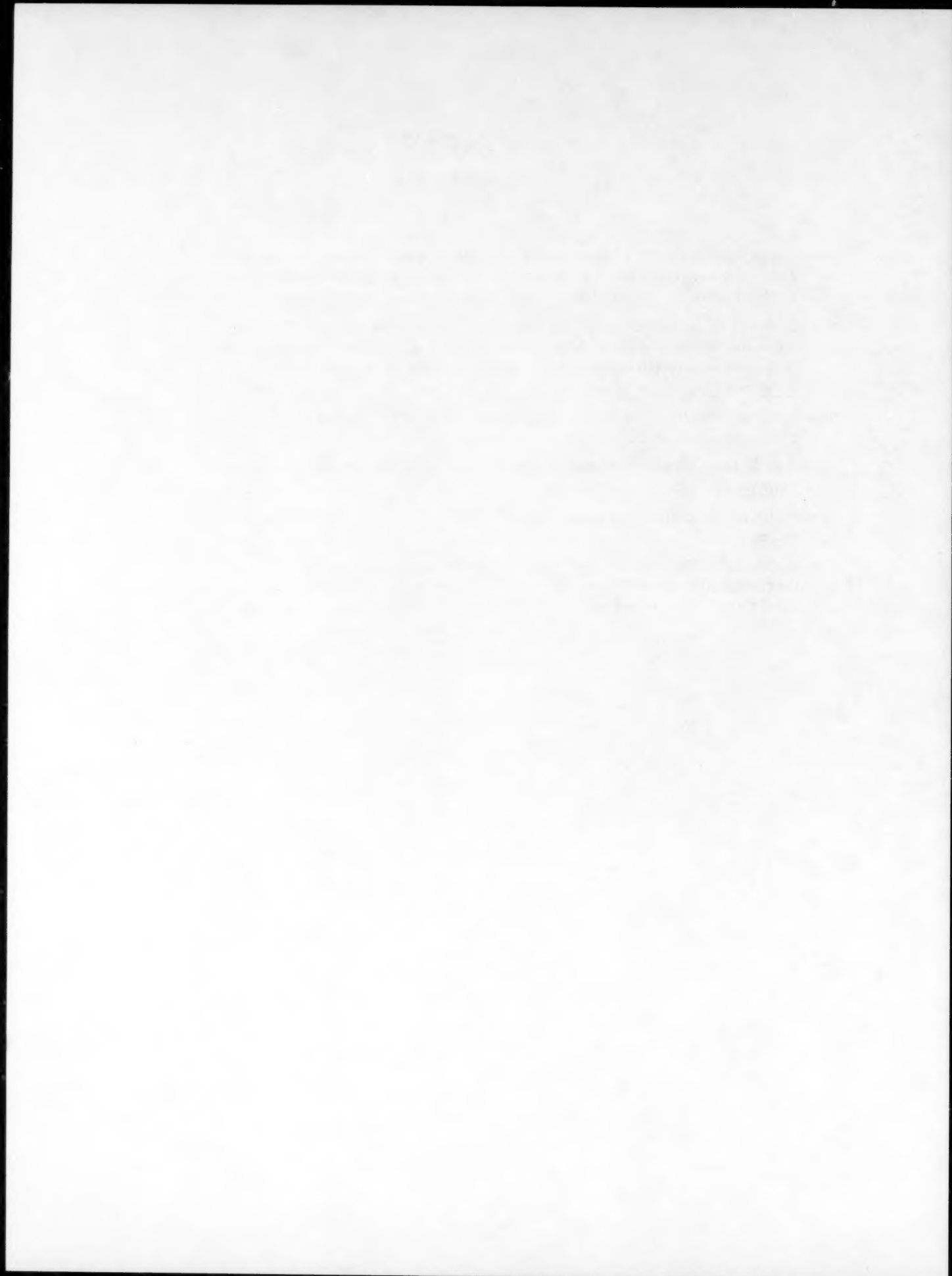
	PAGE	RUSS. PAGE
Interaction of Dialkylphosphorous Acids with Aldehydes and Ketones. XXII. Esters of α -Hydroxy- β , β -dichloroisopropylphosphinic Acid. <u>V. S. Abramov and A. S. Kapustina</u>	3282	3319
Synthesis of Pteridines from 4,5-Diaminopyrimidines and Aromatic α -Keto Acids. II. Investigation of Reaction Between 4,5-Diaminopyrimidines and Phenylpyruvic Acid. <u>S. N. Baranov and T. E. Gorizdra</u>	3285	3322
Synthesis and Conversions of Some Thiazolidine Derivatives. III. Hydrolysis of Azorhodanines. <u>A. P. Grishchuk and S. N. Baranov</u>	3292	3329
Interaction of Piperylene α -Oxides with Hydrogen Chloride. <u>A. N. Pudovik, B. E. Ivanov and Z. M. Zinov'eva</u>	3298	3335
New Method of Synthesizing Esters of Phosphinic and Thiophosphinic Acids. XXXI. Addition of Phosphorous and Hypophosphorous Acids, Dialkylphosphorous Acids and Phosphonoacetic Esters to Maleic Esters. <u>A. N. Pudovik, T. M. Moshkina and I. V. Konovalova</u>	3301	3338
New Method of Synthesizing Esters of Phosphinic and Thiophosphinic Acids. XXXII. Addition of Dialkylphosphorous Acids to Unsaturated Hydrocarbons. <u>A. N. Pudovik and I. V. Konovalova</u>	3305	3342
Amidooximation of the Dinitriles of Adipic and Sebacic Acids. <u>E. N. Zil'berman and N. A. Rybakova</u>	3309	3347
Mechanism of Secondary Amide Formation by the Reaction of Nitriles with Carboxylic Acids. <u>E. N. Zil'berman</u>	3312	3350
Ion Exchange of Complex Salts of Pyridine and Quinoline Bases. <u>I. L. Liplavk and E. P. Boliter</u>	3317	3355
Benz-(c, d)-indoline Derivatives. IV. Condensation Products of 1-Methyl-2-methylthiobenz-(c, d)-indolinium Methylsulfate with 3-Hydroxythionaphthenes. <u>N. S. Dokunikhin, G. M. Oksengendler, and Ya. B. Shteinberg</u>	3323	3361
Chemistry of Cyanine Dyes. XIV. Condensation of Aromatic and Heterocyclic Ketones with Quaternary Salts of 2-Methylbenzthiazole and Conversion of the Compounds Obtained into Cyanine Dyes. <u>I. K. Ushenko</u>	3326	3364
Cyanine Dyes with Unsaturated Substituents. III. Thiocarbocyanines Containing β -Arylvinyl and γ -Phenylbutadienyl Radicals in the 5,5'- and 6,6'-Positions. <u>M. A. Al'perovich, I. K. Ushenko and L. N. Tyurina</u>	3338	3376
Cyanine Dyes with Unsaturated Substituents. IV. Quinocyanines with Phenylbutadienyl and Styryl Radicals in the Quinoline Nucleus. <u>M. A. Al'perovich and I. K. Ushenko</u>	3345	3384
Arylamides of Aliphatic D, L- α -Amino Acids. <u>T. S. Safonova and S. I. Sergievskaya</u>	3353	3391
Radiochromatographic Study of the Formation of Butylenes in the Synthesis of Butadiene by Lebedev's Method. <u>O. M. Vinogradova, G. M. Zhabrova, B. M. Kadenatsi and M. I. Yanovskii</u>	3357	3396
Properties of Trihalomethylsulfenyl Chlorides. <u>K. A. Petrov and A. A. Neimysheva</u>	3362	3401
Dialkyl Phosphates and Pyrophosphates. <u>K. A. Petrov, N. K. Bliznyuk and F. L. Maklyaev</u>	3365	3403

CONTENTS (continued)

	PAGE	RUSS. PAGE
Reaction of Sodium Dialkyl Phosphites with Phosphonates. <u>K. A. Petrov, N. K. Bliznyuk, M. A. Korshunov, F. L. Maklyaev and A. N. Voronkov</u>	3367	3407
Condensation of Ketones with Nitriles Under the Conditions of the Ritter Reaction. <u>A. Ya. Khorlin, O. S. Chizhov, and N. K. Kochetkov</u>	3373	3411
Cycloserine and Related Compounds. VIII. Synthesis of Isoxazolidones-3. <u>N. K. Kochetkov, R. M. Komutov, E. S. Severin, M. Ya. Karpeiskii, E. I. Budovskii, and V. I. Erashko</u> ..	3378	3417
Diaryl Esters of N-Phosphoric Acids of Amidines of the Aromatic Series. <u>G. I. Derkach and A. V. Kirsanov</u>	3385	3424
Conversions of Diazoamino Compounds. III. Homolytic Decomposition of Aromatic Diazo-amino Compounds. <u>V. A. Puchkov</u>	3389	3428
Addition of Nitroalkanes to Dibenzalacetone. <u>S. S. Novikov, I. S. Korsakova and M. A. Yatskovskaya</u>	3394	3433
Replacement of Halogen in Azo Compounds. VIII. Reaction of 2-Chlorobenzeneazo-2'-naphthol with Amines. <u>B. I. Stepanov and L. B. Aingorn</u>	3397	3436
Copolymerization of Poly-1,3-butylene Glycol Fumarate with Allyl Esters of Acids of Phosphorus. <u>S. S. Spasskii and M. E. Mat'kova</u>	3400	3438
Organoboron Compounds. II. Synthesis of Alkylboron Difluorides from Trialkylborons and Boron Trifluoride Etherate. <u>B. M. Mikhailov and T. A. Shchegoleva</u>	3404	3443
Isoxazole Compounds. I. Some Reactions of 3-Methyl-4-benzoyl-5-chloroisoxazole. <u>I. Ya. Postovskii and S. V. Sokolov</u>	3407	3446
Diazo Compounds. XII. Conversions of Diazo Acetate Compounds of Aminoanthraquinones. <u>V. V. Kozlov and B. I. Belov</u>	3412	3450
Method of Preparing 2-Chloroalkyl Esters of Alkylchlorophosphinous Acid. <u>S. Z. Ivin and K. V. Karavanov</u>	3418	3456
Arylaminoanalysis of Aryl Phenylchlorophosphazonesulfones. <u>V. I. Shevchenko and V. T. Stratienko</u>	3420	3458
Polarography of Some Derivatives of Thioxanthene 5-dioxide. <u>I. A. Korshunov and N. I. Malyugina</u>	3425	3463
S-Benzyl Derivatives of Arylthiocarbazonates. <u>R. G. Dubenko and P. S. Pel'kis</u>	3430	3467
S-Methyl Derivatives of Arylthiocarbazonates. <u>R. G. Dubenko and P. S. Pel'kis</u>	3432	3469
Unsymmetrical Organic α -Oxides. XVIII. Condensation Products of Piperylene Oxides with Sodiaoacetoacetic Ester and Acetone. <u>F. G. Ponomarev and N. V. Tinaeva</u>	3435	3471
Preparation of α -Amino Acids from Furan Derivatives. II. Synthesis of Aspartic Acid. <u>A. P. Terent'ev, R. A. Gracheva and V. A. Dorokhov</u>	3438	3474
Synthesis and Properties of Pyrrolidine Bases. VIII. 1-Aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols and Some of Their Derivatives. <u>A. P. Terent'ev, M. A. Volodina, M. L. Smirnova and V. G. Mishina</u>	3443	3478

CONTENTS (continued)

	PAGE	RUSS. PAGE
Investigation of the Properties of Amino Acids and Peptides Containing a Tertiary Nitrogen Atom. I. Simultaneous Decarboxylation and Deamination of N,N-Dibenzyl- α -amino Acid Chlorides. <u>N. A. Poddubnaya and V. I. Maksimov</u>	3448	3483
The Mechanism of the Conversion of α -Acylamido- β -hydroxypropiophenones to the Corresponding Benzoylacetyls. I. Synthesis and Cleavage of α -Benzenesulfonamido- and α -Benzenesulfomethylamido- β -hydroxypropiophenones. <u>V. A. Mikhalev, M. I. Dorokhova and N. E. Smolina</u>	3453	3488
Resin Acids, III. The Nature of High-Melting Abietic Acid. <u>I. I. Bardyshev and O. T. Tkachenko</u>	3457	3493
Preparation of Some Esters of Anabasine-N-formic Acid. <u>G. V. Lazur'evskii and Yu. N. Forostyan</u>	3463	3498
Investigation of the Reaction of Lupinine with Phosgene. <u>G. V. Lazur'evskii and Yu. N. Forostyan</u>	3465	3500
Investigation of the Chemical Structure of the Antibiotic Heliomycin. I. Some Data on the Chemical Nature of Heliomycin. <u>Z. V. Pushkareva, N. M. Voronina, S. I. Omel'chenko, L. B. Radina and Yu. N. Sheinker</u>	3469	3504



INVESTIGATION OF THE EQUILIBRIUM OF THREE LIQUID PHASES IN THREE-COMPONENT SYSTEMS. I

N. I. Nikurashina, R. V. Mertsin, and I. D. Gos'kova

Saratov State University

In present day physicochemical analysis incorrect procedural ideas are still retained on the geometric method of investigating equilibria in various systems. Instead of using this method to obtain a clear reflection of actual phenomena, leading to a particular geometric picture, the exact opposite is often done. By combining pictures obtained experimentally and by introducing arbitrary geometric assumptions, which may not reflect actual phenomena, authors often attempt to "derive" more complicated phase diagrams. This occurs in cases of equilibria of three liquid phases in three-component systems. The scheme for the formation of this equilibrium has not been analyzed at all in modern textbooks on physicochemical analysis. The problem was first posed by Schreinemakers [1], who studied such an equilibrium in the succinonitrile-water-ether system and described it in a general form in his monograph [2]. One of the two schemes given there for the formation of three liquid phases is now included in all textbooks on physicochemical analysis [3].

It is considered that an equilibrium of three liquid phases is possible only with layer formation in all the boundary binary systems. For example in their monograph, V. Ya. Anosov and S. A. Pogodin [3] put forward the incorrect concept that a triangle of three liquid phases is formed by simple intersection of three independent regions of layer formation, which result from binary systems. According to this scheme, three liquid phases may form at a temperature below the critical layer formation temperatures in all three binary systems.

The second system of Schreinemakers [2] presupposes the formation of three liquid phases by the emergence of labile layer formation, located under the stable one, onto the stable binodal layer formation curve. Due to its purely geometric and complex interpretation, the second scheme was forgotten.

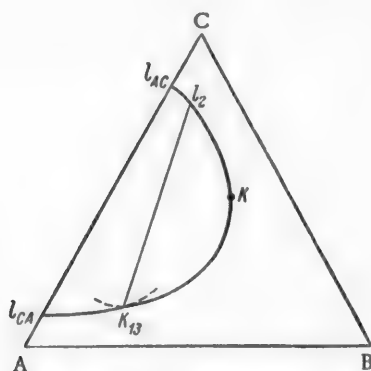


Fig. 1. Appearance of a critical point on the binodal curve.

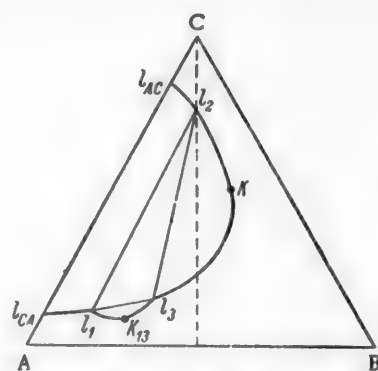


Fig. 2. Appearance of a three liquid phase triangle.

Independently of Schreinemakers, R. V. Mertsin [4] arrived at a scheme similar to the second one: the reasons for the formation of a three liquid phase equilibrium were based not on a geometric construction, but on experimentally confirmed concepts that the interaction between components of a binary system affects the form of the binodal curve. The interaction between components of the predominating binary system is closely connected with the rules governing the distribution of nodes in the layer formation region. This problem was examined thoroughly by Mertsin. He formulated a rule for determining the direction of nodes [5]. The main features of the scheme proposed by Mertsin for the formation of an equilibrium of three liquid phases are as follows.

1. The formation of three liquid phases on the field of layer formation $l_{CA}Kl_{AC}$ (Fig. 1) is related to a loss of predominance in the AB system. Actually, if processes occur in the AB system which lead to layer formation in it, then the weakening of interaction is reflected in the appearance of the critical point K_{12} on the part of the curve turned toward AB. Due to the appearance of the critical point K_{12} , a critical node $K_{12}l_2$ appears on

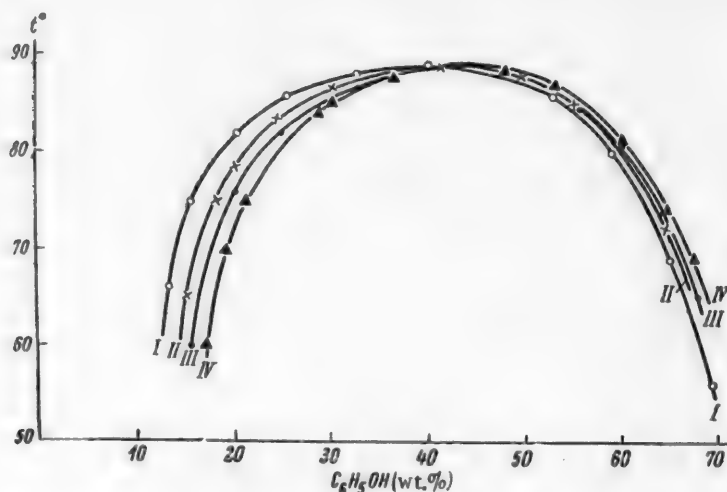


Fig. 3. Horizontal polythermal cross sections in the water-phenol-hexane system. Hexane content (in %) I - 20, II - 40, III - 50, IV - 60.

the layer formation region and with a decrease in temperature this node develops into a triangle of three liquid phases $l_1l_2l_3$ (Fig. 2).

2. The critical node l_2K_{12} (Fig. 1) and the nodal sides of the triangle of three liquid phases, l_1l_2 and l_1l_3 (Fig. 2), should have a direction which coincides with the nodes of the binary layer formation field from which the three liquid phases developed, at least at temperatures that are not very different from the invariant point of the formation of three liquid phases in the system.

From the above one may reach a very important conclusion: three liquid phases may exist at a temperature when in one or even two of the binary systems there is no binary layer formation, i.e., the formation of a three liquid phase triangle is not the result of a mechanical intersection of layer formation fields of all the limiting binary systems. When studying the water-ether-succinonitrile system, Schreinemakers first (1898) observed the existence of three liquid phases at temperatures 2° above the critical layer formation point in the binary system succinonitrile-water. It seemed interesting to obtain new experimental data confirming the accuracy of the scheme proposed for the formation of three liquid phases and the relation of the geometric form of the binodal curve to the direction of the nodal sides of the three liquid phase triangle. For this purpose we investigated the water-phenol-hexane and water-phenol-sulfur systems.

EXPERIMENTAL

The following substances were used for the work: sulfur, recrystallized from freshly distilled carbon disulfide and having m. p. 118° , phenol, doubly distilled with collection of the fraction boiling at 181° , n-hexane, doubly

TABLE 1

Hexane content of ternary system (in wt. %)	Content in water-phenol system (in weight %)		Temp. at which three liquid phases were formed	Hexane content of ternary system (in wt. %)	Content in water-phenol system (in weight %)		Temp. at which three liquid phases were formed
	water	phenol			water	phenol	
20.00	86.90	13.10	66.00 ^c	50.00	80.00	20.00	76.00
20.00	85.00	15.00	75.00	50.00	75.50	24.50	82.00
20.00	80.00	20.00	82.00	50.00	66.80	33.20	87.00
20.00	75.00	25.00	86.00	50.00	59.00	41.00	89.00 [*]
20.00	67.60	32.40	88.00	50.00	50.00	50.00	88.00
20.00	60.00	40.00	89.00 [*]	50.00	44.00	56.00	84.50
20.00	47.00	53.00	86.00	50.00	41.00	59.00	81.50
20.00	40.50	59.50	80.00	50.00	35.50	64.50	74.00
20.00	35.00	65.00	69.00	50.00	33.00	67.00	65.00
20.00	30.20	69.80	56.00	60.00	83.40	16.60	60.00
40.00	85.00	15.00	65.00	60.00	81.00	19.00	70.00
40.00	82.00	18.00	75.00	60.00	79.00	21.00	75.00
40.00	80.00	20.00	78.50	60.00	71.20	28.80	85.00
40.00	75.70	24.30	83.50	60.00	70.00	30.00	85.50
40.00	70.00	30.00	87.20	60.00	64.00	36.00	88.00
40.00	60.00	40.00	89.00 [*]	60.00	58.00	42.00	89.00 [*]
40.00	50.50	49.50	89.00	60.00	51.90	48.10	88.50
40.00	44.50	55.50	85.00	60.00	46.50	53.50	87.00
40.00	35.50	64.50	73.00	60.00	40.00	60.00	81.50
50.00	84.80	15.20	60.00	60.00	32.30	67.70	69.00

^{*} Critical opalescence.

distilled with collection of the fraction boiling at 69° and doubly distilled water. Both ternary systems were studied through layer formation by means of a visual polythermal method [6]. Polythermal cross sections of each ternary system through their temperature - concentration prisms were investigated.

Water - Phenol - Hexane System

The binary systems forming the ternary one were characterized by the following data. The water-phenol system was investigated through its melting point and layer formation [7]. A stable layer formation curve with an upper critical point at 68° was found in it. The water-hexane system shows almost complete insolubility over a wide range of temperatures. The phenol-hexane system was investigated by the authors and showed stable layer formation with an upper critical point at 52°. The ternary system was investigated through four polythermal cross sections with a constant hexane content. During the investigation, a phase transition from a three-phase equilibrium to a two liquid phase equilibrium was observed. The data obtained are given in Table 1 and the solubility isotherms are shown in Fig. 3.

As shown in Fig. 3, all the polytherms have the same form with maxima of intersolubility of the three liquid phases. In all polytherms, critical phenomena were observed between the water and phenol phases, which indicated the formation of a new critical point opposite the binary system water-phenol. Five equilibrium isotherms of the three liquid phases at 68, 80, 85, 88, 89° were plotted from the polytherms obtained. The upper critical point of the three phase state in the system was at 89°, which is 21° higher than the critical point of binary layer formation in the water-phenol system and 37° higher than that of binary layer formation in the phenol-hexane system. Consequently, three liquid phases exist with the presence of two homogeneous binary systems. We were unable to determine the third side of the three liquid phase triangle due to the formation of a stable emulsion, which made it difficult to observe the formation of a third layer. The broken line on the isotherm shows the region of layer formation qualitatively. As Fig. 4 shows, the direction of the critical node and the nodal sides of the three liquid phase triangle is to the left, which agrees with the position of the critical point on the binodal curve.

The critical point is turned toward the binary system hexane-phenol.

TABLE 2

Sulfur content of ternary system (in wt. %)	Content in water-phenol system (in weight %)		Temperature at which three liquid phases were formed	Sulfur content of ternary system (in wt. %)	Content in water-phenol system (in weight %)		Temp. at which three liquid phases were formed
	phenol	water			phenol	water	
20.00	20.40	79.60	67.00°	40.00	49.70	50.30	68.20
20.00	30.50	69.50	71.00	40.00	53.00	47.00	65.00
20.00	40.50	59.50	70.50	60.00	20.30	79.70	63.50
20.00	49.50	50.50	68.00	60.00	23.00	77.00	68.00
20.00	54.10	45.90	63.00	60.00	32.00	68.00	71.00
40.00	19.60	80.40	65.00	60.00	37.50	62.50	70.80
40.00	25.00	75.00	70.00	60.00	48.70	51.30	69.00
40.00	29.70	70.30	71.00	60.00	53.20	46.80	67.00
40.00	38.50	61.50	71.00				

Ternary System Sulfur - Phenol - Water

The binary system phenol-sulfur was investigated by Krupatkin [8] through its melting point and layer formation. He showed that a monotectic equilibrium occurs at 105° and has a high layer formation point and that the layer formation and crystallization curves rise sharply. The binary system sulfur-water shows complete mutual

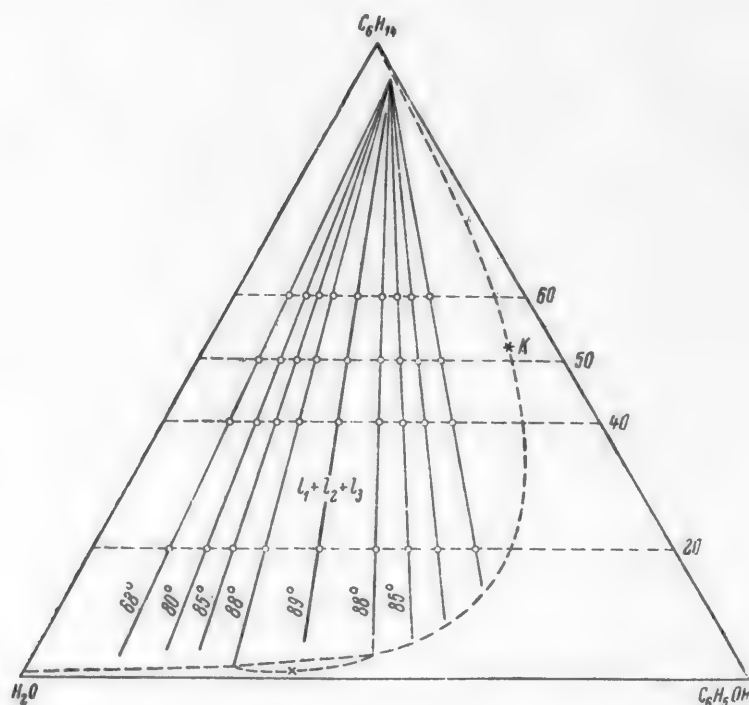


Fig. 4. Equilibrium isotherms of three liquid phases in the water-phenol-hexane system.

insolubility. The ternary system was investigated through three polythermal cross sections with a constant sulfur content. The three liquid phases in this system were in a labile state under the crystallization front of sulfur and therefore, in order to avoid crystallization of the monotectic, supercooling of the mixtures was used for observation. The results are summarized in Table 2 and are shown in Fig. 5. Isotherms at 68, 70, 70.5 and 71° were plotted

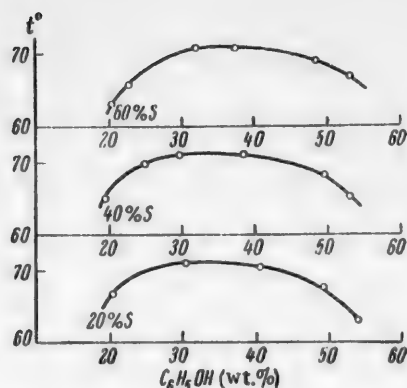


Fig. 5. Horizontal polythermal cross sections in the water-sulfur-phenol system.

tonic character of the solubility lines of the region of two liquid phases and the position of the fictitious critical point, turned toward the sulfur-phenol side.

from the polytherms obtained. We were unable to determine the third side of the three liquid phase triangle as the region of this equilibrium was close to the side of the composition triangle (less than 1% sulfur). However, we may assume that qualitatively it will have the shape shown in Fig. 6 by the broken line at 70°. In addition, the hypothetical lines for the two phase state are shown by broken lines.

All the polytherms have similar layer formation curves with an upper critical point at 71° which is 3° higher than the upper critical point of binary layer formation in the binary system water-phenol. Thus, in this system also the formation of an equilibrium of three liquid phases is not due to a simple intersection of three binary layer formation regions and it exists when there is layer formation in only two of the limiting binary systems.

Fig. 6 shows that the direction of two sides of the triangle and the critical node is to the left and this agrees with the mono-

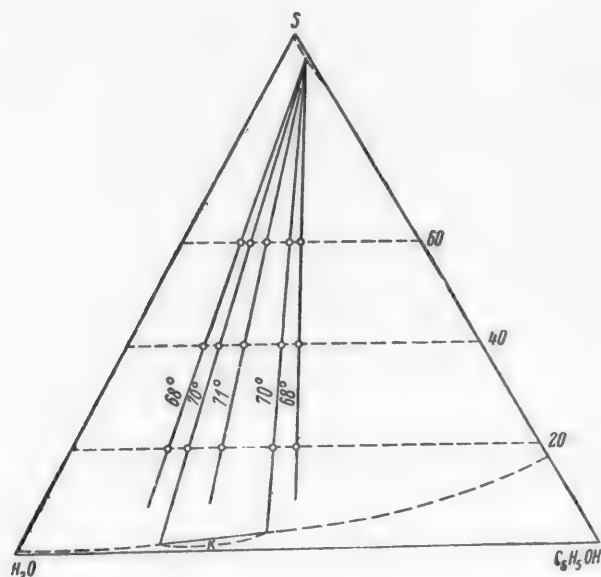


Fig. 6. Equilibrium isotherms of three liquid phases in the water-sulfur-phenol system.

SUMMARY

1. We studied the equilibrium of three liquid phases in the water-phenol-hexane and water-phenol-sulfur systems.
2. A three phase equilibrium was established in the sulfur-phenol-water system at temperatures above the critical point in one of the binary systems and the water-phenol-hexane system at temperatures above the critical point in two of the binary systems.
3. The relation of the direction of the nodes and nodal sides of the three liquid phase triangle in the ternary systems to the position of the critical point in the region of binary layer formation was confirmed experimentally.

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INVESTIGATION OF THE EQUILIBRIUM OF THREE LIQUID PHASES IN THREE-COMPONENT SYSTEMS. II

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The scheme for the formation of a triangle of three liquid phases in ternary systems was described in detail in Report I [1]. The geometric position of this equilibrium triangle on the layer formation region cannot be accidental, but depends on the mutual solubility of all three components. Its location is governed by definite rules on the disposition of nodes on the layer formation region.

In order to obtain new experimental data, we investigated the phenol-water-heptane and sulfur-water-aniline systems.

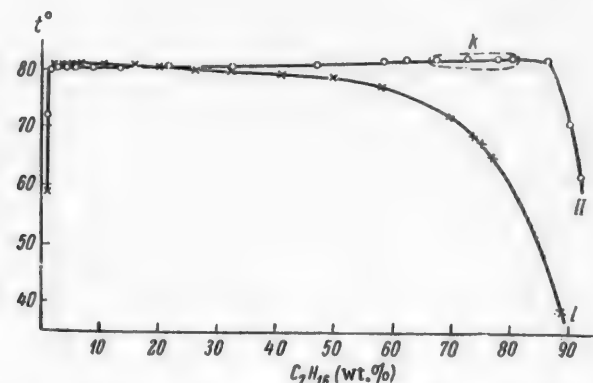


Fig. 1. Vertical cross sections in the phenol-water-heptane system. I) 25% phenol + 75% water, II) 50% phenol + 50% water.

EXPERIMENTAL

The systems were investigated through layer formation by Alekseev's visual polythermal method [2] in sealed glass ampoules in a glycerol thermostat. The following substances were used in the work: sulfur, recrystallized from freshly distilled carbon disulfide and having m. p. 118° , phenol, doubly distilled with collection of the fraction boiling at 181° , purified aniline, doubly distilled with collection of the fraction boiling at 184° , and doubly distilled water.

Phenol - Water - Heptane System

The binary component system water-phenol was investigated by Alekseev [3] through its solubility. The binary system water-heptane shows almost complete mutual insolubility. The binary system phenol-heptane was investigated by the authors of this article and found to show stable layer formation with upper critical point at 53° .

TABLE 1

Content (In wt. %)			Temp. at which three liquid phases form	Content (In wt. %)			Temp. at which three liquid phases form
heptane in the ternary system	phenol in the water system	water in the phenol-water system		heptane in the ternary system	phenol in the water system	water in the phenol-water system	
30.00	11.00	89.00	49.50°	40.00	65.75	34.25	62.30
30.00	17.00	83.00	71.00	50.00	14.80	85.20	58.50
30.00	21.29	78.71	77.00	50.00	19.40	80.60	71.00
30.00	27.86	72.14	81.00	50.00	29.20	70.80	80.00
30.00	37.00	63.00	82.20*	50.00	42.20	57.80	82.50*
30.00	40.00	60.00	82.50	50.00	48.60	51.40	81.90*
30.00	46.86	53.14	81.50	50.00	59.40	40.60	76.00
30.00	53.72	46.28	79.00	50.00	67.80	32.20	62.20
30.00	59.58	40.42	73.50	50.00	73.60	26.40	45.00
30.00	63.29	36.71	67.00	70.00	16.34	83.66	50.00
40.00	13.34	86.66	55.00	70.00	19.67	80.33	60.50
40.00	18.10	81.90	70.00	70.00	26.34	73.66	74.50
40.00	24.67	75.32	78.00	70.00	33.67	66.33	80.60
40.00	27.30	72.70	80.00	70.00	50.00	50.00	82.50*
40.00	33.16	66.84	82.00	70.00	55.00	45.00	81.00
40.00	41.07	58.93	82.50*	70.00	59.34	40.66	78.20
40.00	49.82	50.18	81.20	70.00	65.00	35.00	71.00
40.00	58.21	41.79	75.50	70.00	70.00	30.00	62.00

The ternary system was investigated through four polythermal cross sections with a constant heptane content for each cross section and through two polythermal cross sections of the temperature-concentration prism going from heptane to the water-phenol edge. The numerical data obtained are given in Tables 1 and 2 and the solubility

TABLE 2

Cross section I, 25% phenol + 75% water		Cross section II, 50% phenol & 50% water	
wt. % of heptane in ternary system	temp. at which three liquid phases form	wt. % of heptane in ternary system	temp. at which three liquid phases form
3.10	80.00°	3.70	80.00°
5.20	80.50	5.60	80.20
6.60	80.00	8.60	80.00
10.70	80.50	13.10	80.00
15.70	80.50	21.20	80.50
20.20	80.00	32.30	80.00
25.90	79.70	46.70	81.00
32.10	79.50	58.10	81.50
40.50	79.00	61.60	81.60*
49.30	78.50	66.80	82.00**
57.30	77.00	72.20	82.00**
69.50	72.00	77.70	82.00**
73.10	68.50	80.10	82.50**
74.80	68.00	86.10	82.00
88.50	39.00	90.10	70.80
		91.80	69.00

TABLE 3

Content (In weight %)			Temp. at which liquid phases form
sulfur in ternary system	water in binary system	aniline in binary system	
19.7	9.10	90.90	116.0°
19.9	9.80	90.20	128.0
19.7	10.40	89.60	136.0
20.0	11.30	88.70	147.0
20.0	12.10	87.90	152.0
19.9	87.00	13.00	145.0
19.9	88.30	11.70	135.0
20.0	89.50	10.50	122.0
20.0	90.00	10.00	121.0
20.0	92.00	8.00	110.0
35.1	8.30	91.70	114.0
35.00	9.50	90.50	122.0
35.00	10.70	89.30	136.0
34.95	11.00	89.00	150.0
35.00	85.70	14.30	137.0
35.00	87.60	12.40	127.00
35.02	88.50	11.50	118.0
34.95	90.20	9.80	110.0
35.00	92.00	8.00	100.0
49.80	8.80	91.20	116.0
50.00	9.60	90.40	124.0
49.70	10.30	89.70	139.0
49.0	82.00	18.00	146.0
50.00	84.00	16.00	132.0
50.00	85.50	14.50	121.0
50.00	87.50	12.50	109.0

* Critical opalescence.

** Weak critical opalescence.

polytherms are in Figs. 1 and 2. As Fig. 2 shows, all the polytherms have solubility maxima, which shift toward phenol in going from section I, corresponding to 30% heptane, to section IV, corresponding to 70% heptane. The

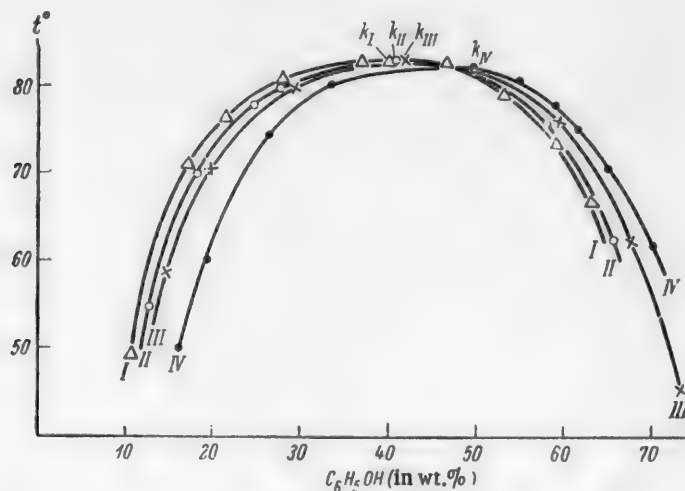


Fig. 2. Horizontal cross sections in the water-phenol-heptane system. Heptane content (in %): I) 30, II) 40, III) 50, IV) 70.

upper critical point on all the cross sections was at 82.5°. Critical opalescence formed in the water-phenol layer, which indicated the appearance of a critical point on the water-phenol side.

The experimental data as well as Fig. 1 show that cross section I with a phenol to water ratio of 15 : 75 does not intersect the critical node, as during the investigation no critical opalescence appeared. However, cross section

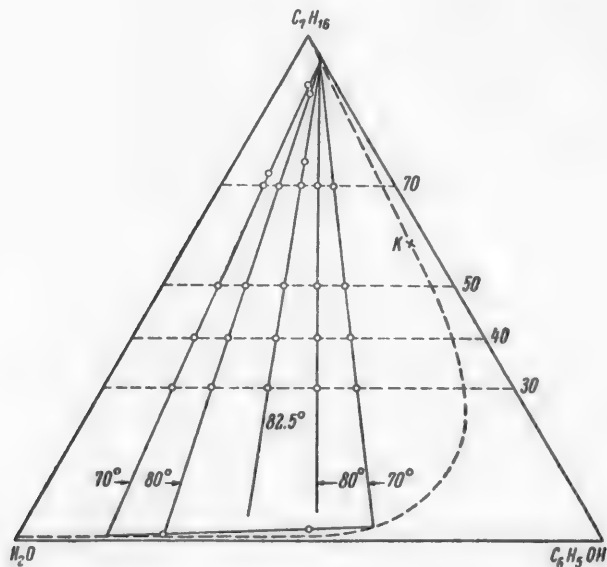


Fig. 3. Equilibrium isotherms of three liquid phases in the water-phenol-heptane system.

II with 50% phenol and 50% water showed critical phenomena over a wide concentration range, which indicated intersection of the critical node. From the polytherms obtained we plotted three equilibrium isotherms of the three liquid phases in the phenol-water-heptane system at 70, 80 and 82.5° (Fig. 3).

As we did not study the two phase equilibrium in the phenol-water-heptane system, broken lines on the composition triangle (Fig. 3) show the hypothetical binodal curve of the region of layer formation. The components of the binary system water-phenol did not indicate any chemical reaction, so the solubility lines of heptane in mixtures of water and phenol do not have extreme points, but show only an increase in the solubility of heptane in passing from water to phenol. The critical point in the layer formation region is turned toward the right to the phenol-heptane system. The critical node and nodal sides of the three liquid phase triangle have the same direction - toward the left, which agrees with the position of the critical point and with the law on the direction of nodes [4].

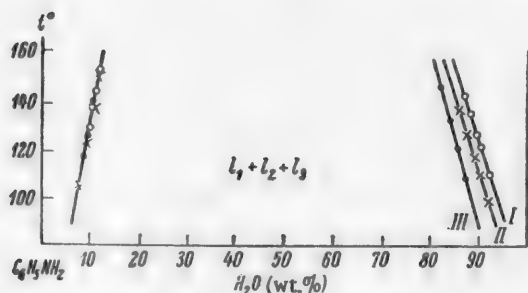


Fig. 4. Vertical cross sections in the sulfur-water-aniline system, I) 20% sulfur + 80% aniline, II) 35% sulfur + 65% aniline, III) 50% sulfur + 50% aniline.

The binary system water-aniline was studied through the solubility of the components in each other [5]. The upper critical point of stable layer formation is at 170°. The binary system sulfur-water showed practically complete mutual insolubility.

The upper critical point of the three phase state in the system is at 82.5°. Three liquid phases form at a temperature 16.5° above the critical point of layer formation in the binary system water-phenol and 29.5° above the critical point in the binary system phenol-heptane.

Ternary System Sulfur - Water - Aniline

The binary systems forming the ternary system are characterized by the following data. The binary system sulfur-aniline was investigated through its melting point. A monotectic crystallizes at 104° and the upper critical point of layer formation is at 139°. The

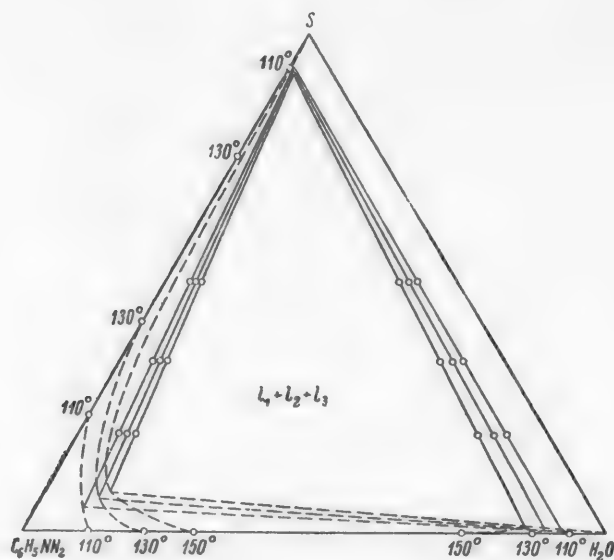


Fig. 5. Equilibrium isotherms of three liquid phases in the water-sulfur-aniline system.

The ternary system sulfur-water-aniline was studied through three polythermal cross sections with constant sulfur contents in each cross section. The temperature at which three liquid phases were formed was determined. The data are summarized in Table 3; the polytherms are shown in Fig. 4.

On all the polytherms, the mutual solubility maxima were located at high temperatures and thus could not be determined; on all the cross sections the mutual solubility of the liquids depended little on temperature and therefore all the solubility curves rose sharply.

From the polytherms we plotted three equilibrium isotherms of three liquid phases at 110, 130, and 150°. Fig. 5 shows the values of the mutual solubility of the components for the binary systems aniline-sulfur and aniline-water at these temperatures. As we did not study the solubility lines of the two phase equilibrium fields, they are shown in the figure by broken lines. We did not study the third side of the three liquid phase triangle and it is shown by broken lines in Fig. 5.

As the upper critical point in the sulfur-aniline system is at 139°, the 150° isotherm shows that binary layer formation breaks away from the binary system sulfur-aniline. At 170°, the second binary layer formation also breaks away from the aniline-water side. One may surmise from the character of the layer formation isotherms of the three liquid phases that the upper critical point of layer formation should lie considerably above the layer formation temperature in the aniline-water system. All these data confirm the theoretical hypothesis that an equilibrium of three liquid phases may be achieved at temperatures when one or two of the binary systems forming the ternary system are homogeneous.

The nodal sides of the three liquid phase triangle l_1l_2 and l_2l_3 have the same direction, namely, to the right, which agrees with the position of the critical point in the region of two phase equilibrium. The critical point is turned toward the left.

SUMMARY

1. We investigated the water-phenol-heptane and sulfur-water-aniline systems through the equilibrium of three liquid phases.
2. It was shown that three phase equilibrium in both systems arises at a temperature above the critical point of layer formation in two of the limiting binary systems.
3. The theoretical concepts of a relation between the geometric position of the three liquid phase triangle and both the character of the layer formation region and the position of its critical point were shown to be correct.

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FIELD OF THREE LIQUID PHASES IN A FOUR-COMPONENT SYSTEM

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The state of three liquid phases in four component systems has not been studied at all. Only one isotherm of the water-ether-potassium iodide-mercury iodide system has been described in the literature [1]. This paper does not contain any generalizations. However, on the basis of the theory of predominance [2] one can readily find not only the basic essential forms of a field of three liquid phases in four-component systems, but also forecast them for any actual system. Let us turn to the derivation of some of them.

In the four-component system ABCD, including one binary layer-forming system AD, let the ternary system ABC be the predominating one. This means that the line of critical points $K_{23}K_{32}$ (Fig. 1) of the region of layer

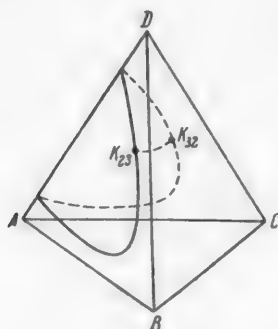


Fig. 1. Line of critical points on the diagram of a four-component system, which includes one binary system with layer formation.

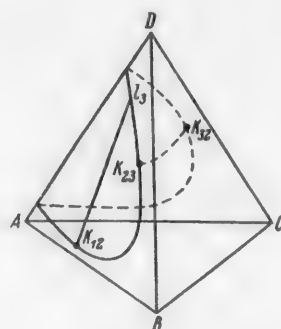


Fig. 2. Formation of a critical node in a ternary system limiting the tetrahedron of a four-component system.

formation is turned toward the plane of the ternary system BCD, while the nodes fan out toward the plane ABC. The appearance of three-phase equilibrium is possible only with the formation of a new system of critical points turned toward the plane ABC. In the simplest case it will arise in the form of a critical node $K_{12}l_3$ in the ternary system ABD (Fig. 2). As the temperature changes, this critical node will begin to move inside the layer-formation region toward the plane ACD and a field of three liquid phases will form behind it. In addition, an independent line of critical points $K_{12}K_{21}$ will form on its own binodal surface. Fig. 3 represents this picture of the state of the system with the field $l_1l_2l_3l'_3K_{21}$ of three-phase equilibrium and the reformed field of two-phase equilibrium with the line of critical points $K_{12}K_{21}$ turned toward the plane ABC. If, inside the field of three liquid phases, we plot the separate triangles of the equilibrium phases, they would together form a fan opening out toward the planes ABC and DBC, which is caused by the presence of the one predominating system BC under these conditions.

One can readily visualize the further deformation of the diagram. Spreading toward the plane ADC, the critical node of the three-phase region will reach the plane at the moment when a three-phase equilibrium will

arise in the ternary system ADC. Now the three-phase region will pass without a break into the tetrahedron from the plane ABD to the plane ACD and the isotherms will correspond qualitatively to Fig. 4.

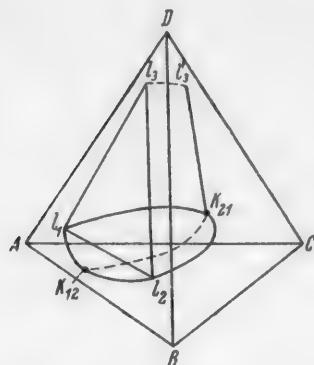


Fig. 3. Formation of a two-phase equilibrium field.

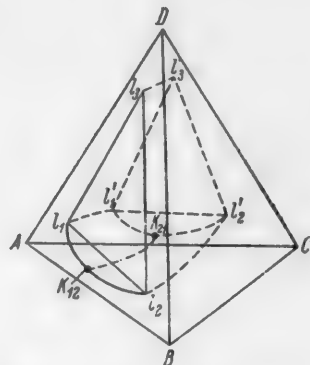


Fig. 4. Region of three-phase equilibrium on the diagram of a four component system.

In order to obtain an accurate idea of the polythermal change in the field of three liquid phases, let us draw a section mm_1m_2 parallel to the plane ABC and in it the sections mx , my and mz from the apex m to the side m_1m_2 (Fig. 5). Let us take the compositions $x_1, x_2, x_3, y_1, y_2, y_3, z_1, z_2, z_3$ in the sections. Let us note the points at which the cross section intersects the sides of the three-phase triangles with gradually changing temperature. The graph given in Fig. 6 will thus be obtained. Before

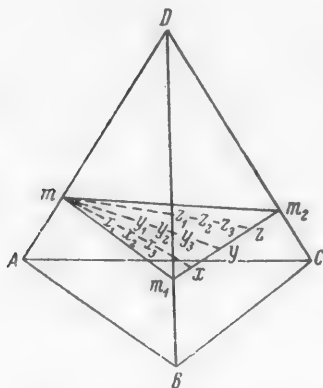


Fig. 5. Construction of a cross section of the diagram.

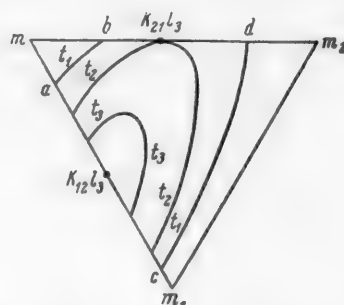


Fig. 6. Isotherms on a cross section of the composition tetrahedron.

reaching the temperature at which the three liquid phases in the system ACD disappear, for example at the temperature t_1 , the isotherm will consist of two separate branches, ab and cd . At the temperature t_2 , at which the three phases disappear in the system ACD, both branches merge at the point of intersection of the critical node $K_{21}l_3$. From this moment the curve will leave the side mm_2 and will be located only within the cross section. It gradually contracts and then disappears in the side mm_1 at the point $K_{12}l_3$. It was stated above that in the four-component system being examined, the binary system BC predominates at all temperatures. Therefore, it would be interesting to obtain a graph of the relation of the maximum temperature at which three liquid phases exist in one or another cross sections of the composition triangle, drawn through the edge AD and various points on the edge BC, to the composition of the predominating system. Using Fig. 6 for this, we obtain the required relation in the form of a continuous curve passing between the temperatures at which the three liquid phases in the ternary systems ABD and ACD disappear and this is shown in Fig. 7. A particular form of this curve may arise as a result of interaction



Fig. 7. Relation of the maximum temperature at which three phase equilibrium exists to the composition of the predominating binary system.

of the components of the predominating binary system and thus an investigation of the field of three liquid phases may be used for physicochemical analysis of binary systems.

Thus, if the predominating binary system includes an undissociated chemical compound V, then there could be three possible cases, depending on whether the temperature of disappearance of the three liquid phases at the composition of the chemical compound is maximum, intermediate or minimum in comparison with the temperatures of the limiting ternary systems. Corresponding diagrams are shown in Fig. 8, where the left diagram corresponds to the first case, the middle one to the second and the one on the right to the last case.

By using the temperature diagrams, one may readily obtain all the qualitative characteristics of the three-phase field isotherms corresponding to them. Let us illustrate this by a case corresponding to the left diagram in Fig. 8. Actually, the presence of a maximum on the temperature curve, corresponding to the chemical compound V, indicates that the field of three liquid phases forms first on cooling and, on the other hand, disappears last on heating in the section ADV (Fig. 9) in the form of the critical node $K_{II}I_3$ with the critical point K_{II} turned toward the plane of the homogeneous ternary system ABC. From this we may conclude directly that the ternary system ABC is a system with an upper ternary critical point. With a decrease in temperature, the critical node $K_{II}I_3$ develops into a triangle of three liquid phases with the formation of a new two-phase field with a critical point K_{AV} , turned toward the line AV. On the right and left of the section ADV will be a field of three liquid phases ending on both sides of it in critical nodes, which at corresponding temperatures will extend to the faces ABD and ACD of the composition tetrahedron.

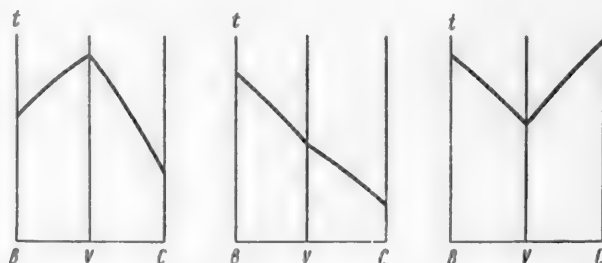


Fig. 8. Different forms of the relation of the temperature at which the three-phase equilibrium disappears to the composition of the predominating binary system.

The case corresponding to the right-hand diagram in Fig. 8 is diametrically opposed to this. The presence of a minimum on the temperature diagram indicates that layer formation in the section ADV will emerge on the isotherm in the form of a critical node, when three liquid phase triangles already exist in the limiting systems ABD and ACD. Therefore, if on the section mm_1m_2 , drawn parallel to the plane of the ternary system ABC, we plot the points of intersection with the triangles of three liquid phases, we obtain Fig. 10. It shows that the three-phase state will disappear first in the section mx at a temperature t_4 and a composition x, which corresponds to the ratio of the components in the predominating system, characteristic of compounds V. As the temperature increases, the field of three liquid phases will contract on both sides of section mx and this is shown in Fig. 10 by the appearance of two separate systems of curves, which correspond to the increasing temperatures t_3 , t_2 and t_1 , and disappear separately at sides mm_1 and mm_2 on reaching the temperatures at which the three liquid phases disappear from the limiting ternary systems.

We examined the simplest case when a four-component system included one binary predominating system. However, this does not always occur. It may happen that the four-component system is at a stage when predominance passes from one binary system to others. Let us limit ourselves to the examination of one possible case. Let

us again examine Fig. 4. Let us suppose that with a change in the equilibrium parameters (pressure and temperature), in the four-component system ABCD the interaction between components B and C will weaken, but the interaction between A and B, on the one hand, and C and D, on the other, will increase.

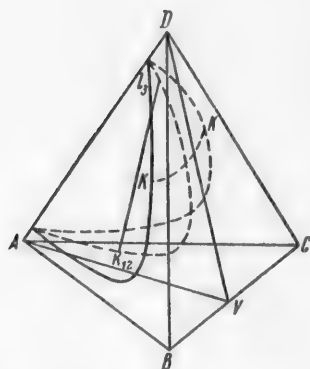


Fig. 9. Isotherms of a three-phase field in the composition tetrahedron.

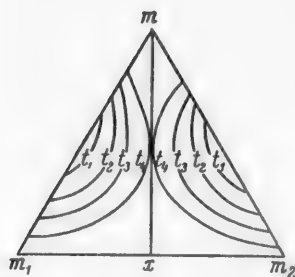


Fig. 10. Isotherms of a three-phase field in the composition tetrahedron (another case).

Corresponding changes will then occur in the form of the triangles of three liquid phases; on the face ABD the triangle will extend toward the edge AB, and on the face ADC it will extend toward the edge CD. If component C is now introduced into the system ABD, this will gradually weaken the effect of the interrelation of the components AB and increase the effect of the interrelation of the components DC. On the other hand, if component B is introduced into the ternary system ADC, we will increase the effect of the interrelation of the components AB and decrease the effect of the interrelation of the components CD. The first process is expressed geometrically by the gradual widening of the triangle of three liquid phases on the side turned toward the plane ABC; the second is expressed by the widening of the side turned toward the plane BCD. Thus, if with further deformation of the field of three liquid phases, the points l_1' and l_2' merge with the formation of the critical node $K_{12}l_3$ on the face ABD and the points l_2' and l_3' merge into the critical node $K_{23}l_1'$ on the face ACD, the field of three liquid phases will remain inside the tetrahedron.

As the qualitative compositions of the two terminal critical nodes are different (one of them has the critical point K_{12} , formed by the first and second phases and the other has the critical point K_{23} , formed by the second and third phases), they cannot disappear by superposition of one on the other to form a single critical node. Therefore, one must assume that with continuing deformation, with a decrease in the three liquid phase volume within the tetrahedron bounded by critical nodes, these nodes will gradually decrease. At the moment when the three-phase field disappears, both terminal critical nodes will decrease to critical points and will merge into a single ternary critical point K_{123} (Fig. 11) in which all three phases are identical in composition and properties. Only one single curve of the critical points K_{12} , K_{123} and K_{23} will remain on the surface of layer formation. In order to find the ternary critical point we must examine the polythermal picture of the tetrahedron sections drawn parallel to the plane ABC. For this purpose let us use Fig. 12, which gives a composition tetrahedron for the system ABCD and on its faces ABD and ACD are drawn the three liquid phase triangles $l_1l_2l_3$, which have a configuration corresponding to the case examined. It is readily established that the character of the curves of the intersections with the sides of the liquid phase triangles will change not only with temperature, but also

with the height of the section in the tetrahedron, i.e., with content of component D.

Actually, let us construct section mm_1m_2 (Fig. 12) in such a way that it intersects the sides l_1l_3 and l_2l_3 of the triangle on the face ABD at points a and b . As our section intersects the sides l_1l_3 of the triangle on the face ACD at points c and d , then consequently, there will always be inside the tetrahedron a triangle which will be intersected by our section directly at the point corresponding only to phase l_2 . Thus, the diagram of the cross section given in Fig. 13 will have the curve ac , which corresponds to a two-phase state l_1l_3 and the curve bd with the point l_2 on it dividing the part of the curve bl_2 , corresponding to the two-phase state l_2l_3 , from the part l_2d , corresponding to the two-phase state l_1l_2 .

If a section is chosen that is located above the one examined, its picture will be qualitatively the same, but point l_2 will be displaced toward point d . On reaching it the section will also intersect the sides l_1l_3 and l_2l_3 of the triangle on the face ACD. On the other hand, with a decrease in the content of component D, the point l_2 will move toward point b . On reaching it, the cross section will intersect the triangle only at the sides l_1l_2 and l_1l_3 . Such are the possible isotherms.

Let us turn to the polytherms. Let us increase the temperature. Then the points l_1 and l_2 on the face ABD (in section a and b) and l_2 and l_3 on the face ACD (in section c and d) will move toward each other and at certain temperatures will separately produce critical nodes $K_{12}l_3$ and $K_{32}l_1$, respectively, which will move from the faces into the tetrahedron. Thus, a closed loop (Fig. 14) including the points $K_{12}l_3$ and $K_{32}l_1$, will appear on the section and, depending on the height of the section and the relative disposition of the

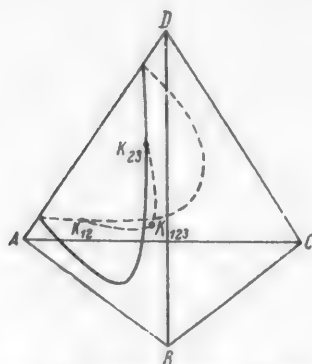


Fig. 11. Disappearance of the three-phase field and the formation of a ternary critical point.

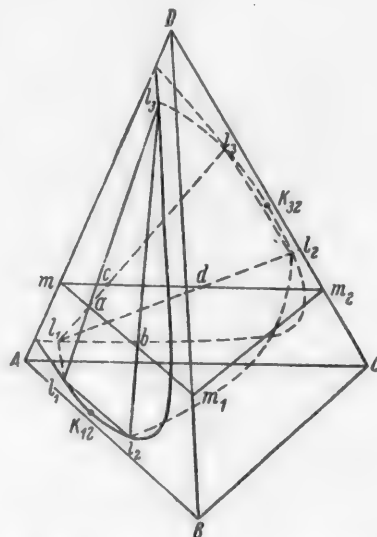


Fig. 12. Construction of sections for finding the ternary critical point.

critical nodes in the tetrahedron, the points $K_{12}l_3$ and $K_{32}l_1$ will include the critical phases K_{12} and K_{32} in different weight ratios with the phases l_3 and l_1 . We noted above that with an increase in temperature the critical nodes decrease in length and their critical points approach each other. Therefore, in the sections we should observe the

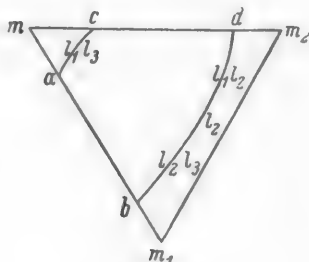


Fig. 13. Isotherms of a two-phase state on a cross section of a composition tetrahedron.

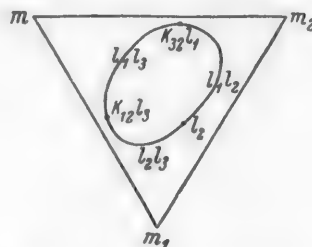


Fig. 14. Closed isotherms on a cross section of a composition tetrahedron.

disappearance of the critical points from the loops as soon as the critical nodes emerge from these sections. Without the critical points, the loop continues to contract, and the field of three liquid phases disappears at a definite temperature for the given section, which is lower than the temperature of the ternary critical point.

If the section contains a composition which corresponds to the ternary critical point, then, evidently, the field of three liquid phases of this section will disappear at a temperature higher than that of other sections and both the points $K_{12}l_3$ and $K_{32}l_1$ will remain on the loop which contracts with an increase in temperature. The

amount of phases l_2 and l_1 decreases and when the temperature of the ternary critical point is reached, these phases disappear completely. The remaining critical phases K_{12} and K_{23} will merge to form a single ternary critical point K_{123} .

SUMMARY

1. The problem of the field of three liquid phases in some four-component systems has been examined.
2. It was shown that the interaction of the components of the predominating binary system is reflected on the surface of the volume of three liquid phases.
3. The problem of temperature deformation of the field of three liquid phases was examined.

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SYSTEMS WITH A LOWER TERNARY CRITICAL POINT

I. LAYER FORMATION IN THE CHLORAL HYDRATE-WATER-PYRAMIDON SYSTEM

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Fig. 1 shows the phase diagram of a ternary system with a break in the solubility of the liquid phases, which, in the theory of heterogeneous equilibria, is regarded as a diagram of a general type. We showed previously [1] that its upper section forms only with quite definite physicochemical relations between the components of the system, namely, when one of the limiting binary systems shows chemical interaction of the components. The other two limiting systems could have limited or full solubility of the components in the liquid state.

Neither the complete phase diagram of a general type of system, nor examples of systems with a lower ternary critical point have been found experimentally. We do not propose to contradict Schreinemakers' theoretical point of view that there is a possibility that ternary systems of a general type and systems with a lower ternary critical point of layer formation may actually exist. On the contrary, using physicochemical analysis as previously, we will complete the purely geometric scheme given by Schreinemakers and show the conditions of component interaction necessary for realizing such systems.

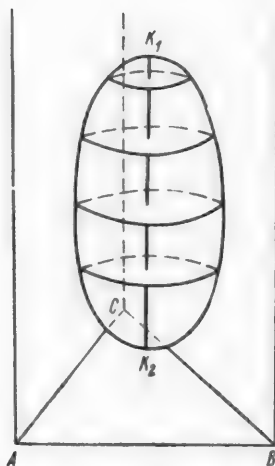


Fig. 1. Phase diagram of a ternary system with a break in the solubility of the liquid phases.

If one takes the phase diagram of a ternary system of the general type (Fig. 1) and mentally draws planar cross sections passing through points of different component ratios in the binary system A-B and the temperature axis of the third component C, then such separate cross sections will correspond to a phase diagram of a binary system with a closed region of layer formation. Some consider that binary systems with a closed loop for the region of layer formation, as well as the particular case of systems with a lower critical solution point, must also be systems in which there is chemical interaction of the components. This is confirmed by measurements of various physical properties of such systems as well as the isolation, in individual cases, of crystalline products of mutual association of the components (chloral hydrate, bromal hydrate, butylchloral hydrate etc.). In systems with a lower critical point there is apparently a mobile chemical equilibrium of the form: $A + B \rightleftharpoons AB$. A shift of this equilibrium in a forward direction leads to homogenization of the system and a shift in the opposite direction leads to layer formation.

It seemed to us that the above was fully applicable to the planar cross sections of a ternary system of the general type. To obtain the required geometric picture of the cross section, it is necessary to assume that the complex of the prevailing limiting system A-B with the third component C of the ternary system

forms a thermally unstable chemical compound. At low temperatures, when the thermal dissociation of this compound is still low, the compound acts as a homogenizer of the components forming it. An increase in temperature leads to decomposition of the chemical compound, to a decrease in its concentration in the ternary complexes, to an increase in the concentration of its decomposition products and, consequently, to a break in the solubility of the liquid phases.

However, as the limiting binary system A-B is itself a system with chemical reaction (if the contrary was the case, then layer formation with an upper ternary critical point could not occur in the ternary system) then the lower part of the phase diagram of the general type requires chemical interaction between this binary compound and the third component. In brief, the ternary system must have a ternary compound, which decomposes by the reaction: $ABC \rightarrow AB + C$.

However, decomposition of the ternary chemical compound would not always lead to a break in solubility in the system. It may happen that a system includes a ternary compound but no layer formation occurs in it. We consider that it is precisely this type of ternary liquid system which, with interaction of the components, would be most common. The contrary would occur when the binary compound AB, having a different physicochemical nature from that of its components, would mix in a limited way with the third substance of the system, C. Only under these conditions could one expect layer formation in a system with a lower ternary critical solution point. Here the ternary compound must act as a homogenizer with respect to layer formation between AB and component C.

Experiment has shown that ternary chemical compounds are primarily found in those ternary systems in which all three limiting systems are characterized by chemical interaction of components.

EXPERIMENTAL

The most probable method of finding a phase diagram of this type was to select components with the physicochemical relationship mentioned above. It seemed to us that this occurs in the ternary system chloral hydrate-water-pyrimidon. From literature data it is known that all three substances forming this ternary system form with each other binary systems with chemical interaction of the components.

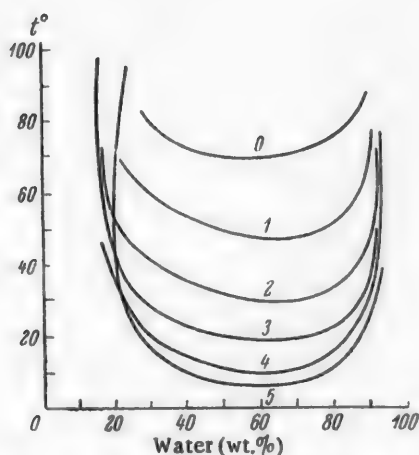


Fig. 2. Polythermal cross sections of the chloral hydrate-water-pyrimidon system. 0) Without chloral hydrate; ratio of chloral hydrate to pyrimidon: 1) 0.1, 2) 0.2, 3) 0.3, 4) 0.4, 5) 0.5.

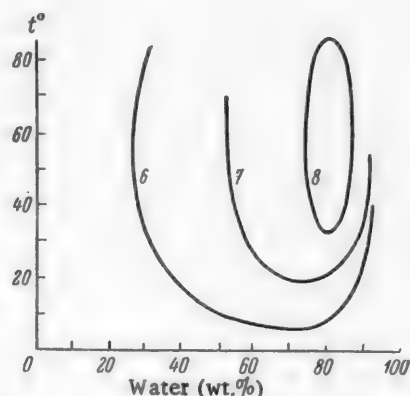


Fig. 3. Polythermal cross sections of the chloral hydrate-water-pyrimidon system. Ratio of chloral hydrate to pyrimidon: 6) 0.6, 7) 0.7, 8) 0.8.

Pyrimidon-water system. The mutual solubility of pyrimidon and water was first studied thoroughly in [2]. It was found that this system has a closed region of layer formation. According to the authors experimental data, the lower critical solubility point of the liquid phases was at 70° and the upper one at 190°. The solubility of the solid phases of the system was studied by S. I. Kaplan and F. E. Rabinovich [3] and according to their data, this system is of a monotectic type with a strongly developed field of pyrimidon crystallization. The monotectic line intersects the layer formation field at 73° and draws the lower section of the field into a region of metastable equilibrium. The unusual form of the phase diagram of the system is apparently closely related to the chemical

interaction of the components. However, due to the very low heat effect of the chemical reaction, the hydration products of pyramidon formed decompose when the temperature is raised.

The chloral hydrate-water system was investigated through the melting point by Van Rossem [4]. He established that it contained a crystal hydrate with the composition $\text{CCl}_3\text{COH} \cdot 7\text{H}_2\text{O}$ and m. p. -1.4° . The specific gravity and viscosity of this system were measured by N. S. Kurnakov and N. N. Efremov [5]. As these investigators stated the liquid system chloral hydrate-water is a typical example showing the effect of hydration processes on the form of the isotherms of the properties mentioned above. With a decrease in temperature, the irrational maxima of the physical property isotherms are displaced toward chloral hydrate. Finally, investigations carried out by Werner [6] and Van Rossem [4] established that layer formation occurred with chloral hydrate and its separate solutions in water and also with chloral on heating in sealed ampoules to 180° . Thus, chloral hydrate, being a reaction product of chloral and water, is itself in a state of dissociation in a liquid medium and this is greater the higher the temperature and the less active the mass of reacting substances.

There is no information in the literature on the third binary system pyramidon-chloral hydrate. Nonetheless, in analogy with the antipyrine-chloral hydrate system [7], one may expect chemical interaction of the components here.

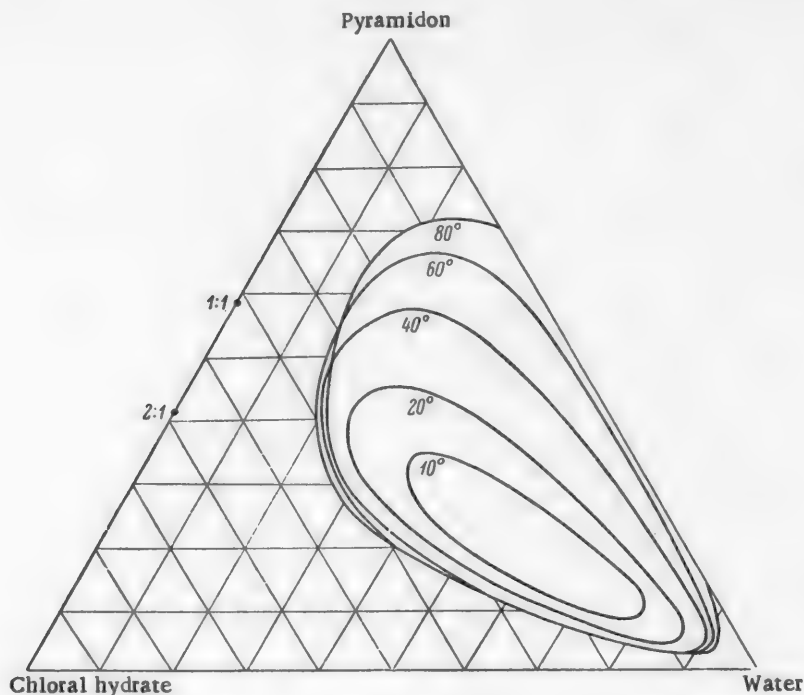


Fig. 4. Projection of isotherms of the layer formation region on the composition triangle of the system.

In this work we used pharmaceutical grade pyramidon and chloral hydrate and doubly distilled water.

The temperature and concentration limits of the layer formation region in this system were investigated by V. F. Alekseev's polythermal method [8]. The concentration composition triangle of the system was cut by lines which passed through definite ratios of the components of the binary system pyramidon-chloral hydrate to the apex corresponding to the third component of the system, water. Solutions corresponding to these lines were prepared and these had component ratios which made it possible to fully characterize the layer formation polytherm. A total of 8 sections of the ternary system were made: the chloral hydrate content of binary mixtures of it with pyramidon were 10, 20, 30, 40, 50, 60, 70 and 80 weight %.

As well as these sections of the ternary system, we also investigated the layer formation region in the binary system pyramidon-water. Our results agreed completely with experimental data in [2].

In view of the problem in hand, we did not attempt to follow the full course of the polythermal curves. When the temperatures at which layer formation began was over 100°, we terminated our observations.

As the numerical material on the investigation of the binary system pyramidon-water and that of the polythermal sections of the ternary system is very voluminous, it is given graphically. Figures 2 and 3 show the polythermal curves of sections of the ternary system that were plotted from the experimental data obtained. Here the water content of the mixtures investigated is plotted along the abscissa and the temperature at which layer formation started, along the ordinate. The zero curve corresponds to the lower part of the layer formation region in the binary system pyramidon-water. Figure 4 shows separate isotherms of the layer formation region of the system and these were plotted using polythermal curves and a graphical interpolation method.

DISCUSSION OF RESULTS

The experimental material we obtained indicates that layer formation in the ternary system pyramidon-water-chloral hydrate occurs at temperatures below the lower limit of the layer formation region in the binary system pyramidon-water. Above 69° the two liquid phase state region adjoins the pyramidon-water edge of the composition triangle and below this temperature it separates from the edge and passes into the volume of the concentration triangle of the system. The latter is seen very clearly from the isothermal lines (Fig. 4) which separate the region of a heterogeneous liquid state from that of homogeneous solutions. With a decrease in temperature, the isothermal lines contract noticeably with a clear decrease in their capacity to encompass concentrations of ternary solutions and at 5° the lines become a point. Thus, by studying the mutual solubility of liquid phases in the pyramidon-water-chloral hydrate system, we were the first to show experimentally the actual existence of three-component systems with a lower ternary critical point. This problem was solved successfully by physicochemical analysis.

The original disposition of the isothermal lines of the layer formation region is noteworthy. They are all extended toward the limiting binary system chloral hydrate-pyramidon. In accordance with the concept of predominating systems, we must consider this binary system as the one with the most strongly expressed chemical interaction of the components. With changing temperature, the large diameters of the concentric isotherms of the layer formation region move in succession from the limiting system chloral hydrate-water toward the limiting system pyramidon-water. This indicates, on the one hand, the irrational character of the predominating system, and, on the other, the presence of several addition products in it. If the large diameters of the layer formation region isotherms at low temperatures are extended to the chloral hydrate-pyramidon side, they indicate a component ratio of $C_{13}H_{17}ON_3 \cdot 2C_2Cl_3H_3O_2$, while at higher temperatures, this ratio becomes more clearly $C_{13}H_{17}ON_3 \cdot C_2Cl_3H_3O_2$. One may consider that the chloral hydrate-pyramidon system contains several thermally dissociated compounds, of which the 1 : 1 compound is probably most stable.

In polythermal sections (Figs. 2 and 3) characterized by high chloral hydrate contents, the lines of limiting solutions of the two-phase liquid state start to draw together with an increase in temperature. Although in the first sections, the closing of the binodal curves in the temperature range being investigated was not observed very clearly, in subsequent sections it became quite clear. Finally, in the last section (80 weight % of chloral hydrate) the heterogeneous state region has both a lower and an upper critical solution point. Apparently, all the other polythermal sections show a similar picture.

This form of binodal curve indicates that the ternary system includes two independent layer formation regions, of which one adjoins the limiting system, pyramidon-water and the other, the chloral hydrate-water system.

SUMMARY

1. Layer formation in ternary system chloral hydrate-water-pyramidon was studied.
2. It was shown that this system has a layer formation region with a lower ternary critical solution point.
3. The existence of such systems was proved for the first time by investigating the chloral hydrate-water-pyramidon system. The most probable condition for their formation is chemical interaction between all three components, which results in the formation of thermally dissociated ternary compounds in the system.

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TERNARY RECIPROCAL SYSTEM OF SODIUM AND POTASSIUM ACETATES AND CAPROATES

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The $\text{Na}_2\text{K} \parallel \text{CH}_3\text{COO}, \text{C}_6\text{H}_{11}\text{COO}$ system completes the series of systems of sodium and potassium acetates and salts of other aliphatic acids that we have studied for the general purpose of establishing a relation between the direction of an exchange reaction and the structure of the salt radical.

The melting points of the starting materials were as follows: sodium acetate 331° [1], potassium acetate 301° [1], sodium caproate 365° [2] and potassium caproate 444.5° [3]. The starting salts undergo polymorphic conversions: sodium acetate at $58, 118, 130$ and 238° [3], potassium acetate at 58 and 155° [3], potassium caproate at 302° [3] and sodium caproate at $203, 226$ and 342° [3]. All the salts melt without decomposition.

EXPERIMENTAL

For the investigation we used the normal procedure of visual-polythermal physicochemical analysis. Chemically pure grade potassium and sodium acetates were used for the work, while the potassium and sodium caproates were synthesized by the method described previously [2]. All compositions are expressed in molecular percents.

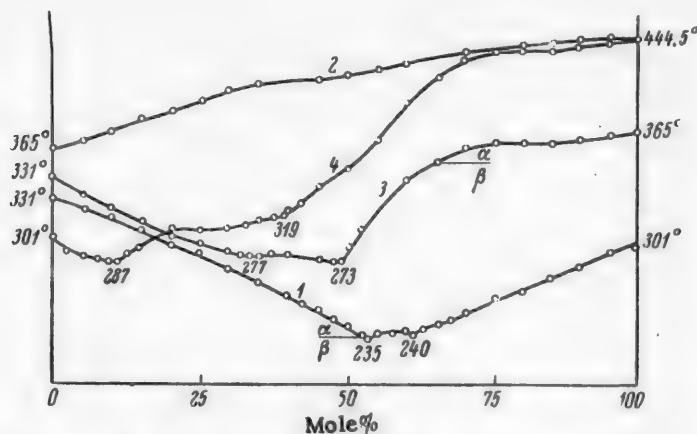


Fig. 1. Sides of the square of the ternary reciprocal system.

Binary Systems (Fig. 1)

1. $\text{CH}_3\text{COONa} - \text{CH}_3\text{COOK}$ had been studied previously [4]. A complex compound forms in the melt [1]. The three branches of the melting point curve intersect in two eutectic points at 235° and 53.5% of potassium acetate and 240° and 61.5% potassium acetate.

2. $C_6H_{11}COONa-C_6H_{11}COOK$ forms a continuous series of solid solutions without an extremum on the melting point curve.

3. $CH_3COONa-C_6H_{11}COONa$ was first described by N. M. Sokolov [2] and reinvestigated by us. A complex compound is formed here and its approximate composition is $4CH_3COONa \cdot C_6H_{11}COONa$. The three branches of the melting point curve intersect in a eutectic point at 273° and 48.5% of sodium caproate and a transition point at 277° and 34.0% of sodium caproate.

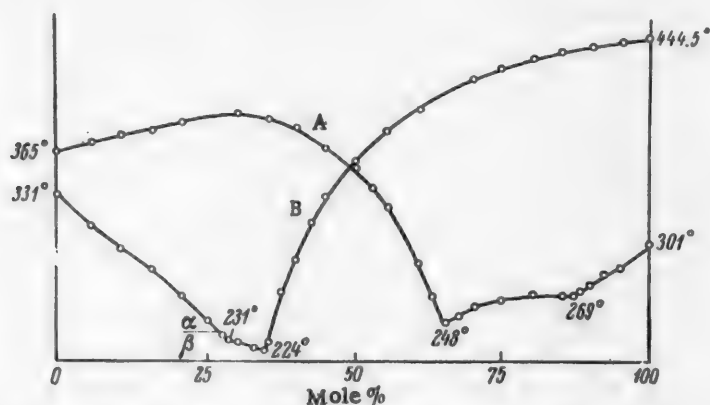


Fig. 2. Diagonal cross sections of the system. A) $C_6H_{11}COONa-CH_3COOK$, B) $CH_3COONa-C_6H_{11}COOK$.

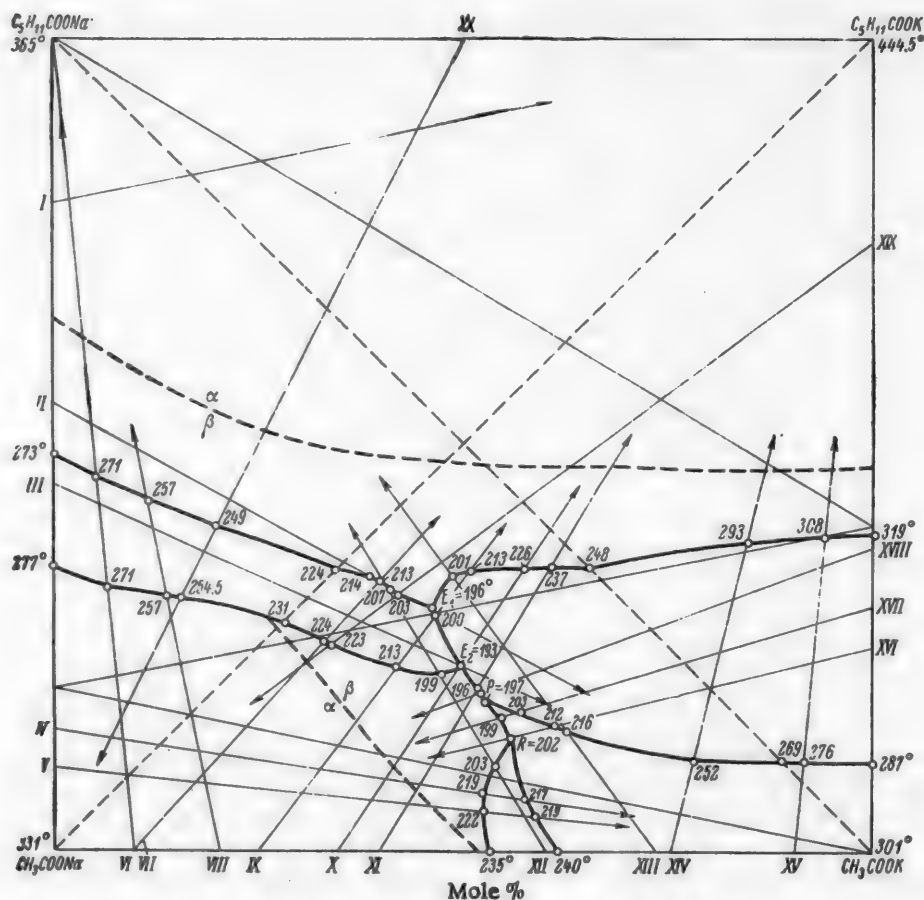


Fig. 3. Disposition of internal cross sections in the system $Na, K \parallel CH_3COO, C_6H_{11}COO$.

4. $\text{CH}_3\text{COOK} - \text{C}_5\text{H}_{11}\text{COOK}$ was first investigated by N. M. Sokolov [5]. Our data confirmed the presence of a complex compound. The three branches of the melting point curve intersect in a eutectic point at 287° and 11.0% of potassium caproate and a transition point at 319° and 39.0% of potassium caproate. The approximate composition of the complex compound is $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK}$.

Diagonal Cross Sections (Fig. 2)

1. The diagonal cross section $\text{C}_5\text{H}_{11}\text{COONa} - \text{CH}_3\text{COOK}$ passes through the field of solid solutions of sodium and potassium caproates, the field of the compound $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK}$ and the field CH_3COOK ; the melting point curve has three branches which intersect in points at 248° and 65.0% of potassium acetate and 269° and 88.5% of potassium acetate.

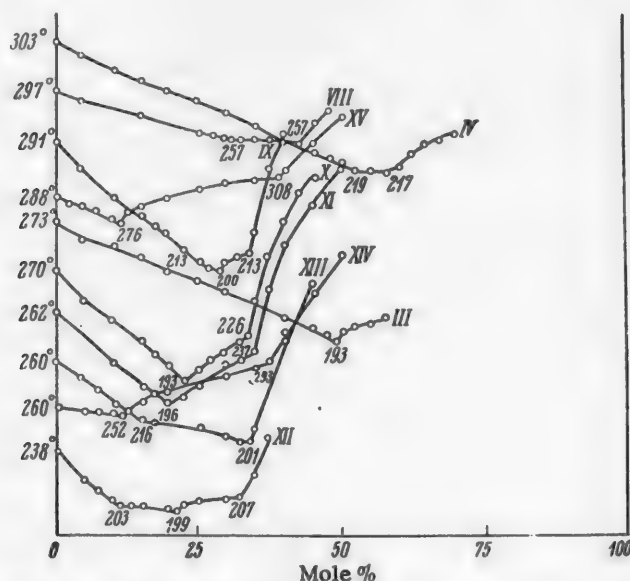


Fig. 4. Internal cross sections of the ternary reciprocal system Na, K || CH_3COO , $\text{C}_5\text{H}_{11}\text{OO}$.

2. The diagonal cross section $\text{CH}_3\text{COONa} - \text{C}_5\text{H}_{11}\text{COOK}$ passes through the field of CH_3COONa , the field of the compound $4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa}$ and the field of solid solutions of sodium and potassium caproates. The three branches of the melting point curve intersect in points at 231° and 28.0% of potassium caproate and 224° and 34.5% of potassium caproate. Both diagonal cross sections are unstable. The system is of the adlagonal-zone type.

Internal Cross Sections

20 internal cross sections in reciprocal systems were investigated and their direction is shown in Fig. 3; their characteristics are given in Figs. 4 and 5.

Crystallization Surface of the System. The three-dimensional diagram of the reciprocal system is projected onto the composition square in Fig. 6. The reciprocal system diagram is divided by the cocrystallization lines into six fields (in % of the total liquidus surface of the ternary reciprocal system): I field of sodium and potassium solid solutions, 63.4; II field of CH_3COONa 14.2, III field of the compound $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK}$ 11.8, IV field of CH_3COOK 5.1, V field of the compound $4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa}$ 4.9, and VI field of the compound $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COONa}$ 0.6.

The two complex compounds $4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa}$ and $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK}$ on opposite sides of the square of the system, make it possible to divide the square into two tetragons, which in their turn are divided into phase triangles. The compound $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COONa}$ has a triangular field with a transition point R at 202° and 55.5% potassium acetate, 14.0% sodium caproate and 30.5% sodium acetate.

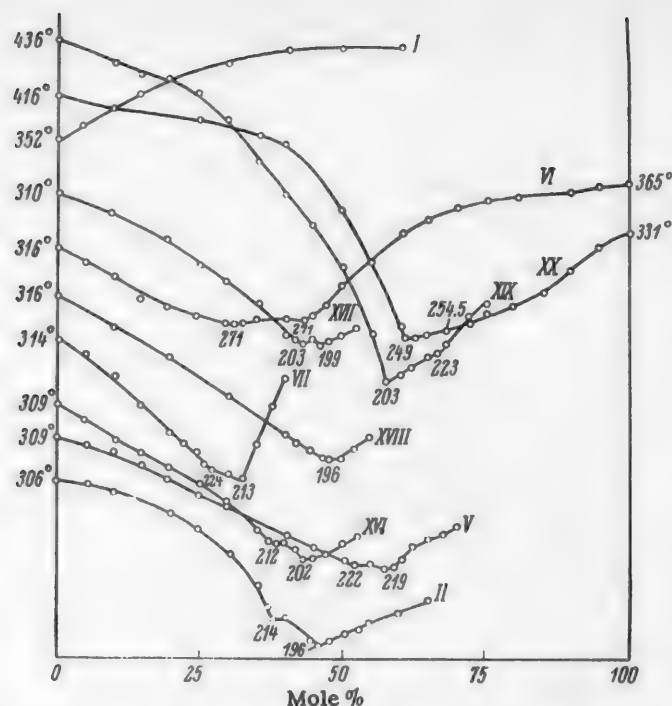


Fig. 5. Internal cross sections of the ternary reciprocal system $\text{Na, K} \parallel \text{CH}_3\text{COO, C}_5\text{H}_{11}\text{COO}$.

The first tetragon $4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa} - 3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK} - \text{C}_5\text{H}_{11}\text{COOK} - \text{C}_5\text{H}_{11}\text{COONa}$ is divided by the secant from the hypothetical compound $3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK}$ into two phase triangles: 1) $4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa} - 3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK} - \text{C}_5\text{H}_{11}\text{COONa}$ with a eutectic point E_1 at 196° and 29.5% sodium caproate, 46.0% potassium acetate and 24.5% sodium acetate; 2) $\text{C}_5\text{H}_{11}\text{COONa} - 3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK} - \text{C}_5\text{H}_{11}\text{COOK}$ phase triangle corresponds to a continuous series of solid solutions of sodium and potassium caproates.

The second tetragon, $\text{CH}_3\text{COONa} - \text{CH}_3\text{COOK} - 3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK} - 4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa}$ is also divided into two phase triangles. The melts included in the third phase triangle, $\text{CH}_3\text{COOK} - 4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa} - 3\text{CH}_3\text{COOK} \cdot 2\text{C}_5\text{H}_{11}\text{COOK}$, solidify at a eutectic point E_2 at 193° and 49.5% potassium acetate, 22.5% sodium caproate and 28.0% sodium acetate. The fourth phase triangle, $\text{CH}_3\text{COONa} - 4\text{CH}_3\text{COONa} \cdot \text{C}_5\text{H}_{11}\text{COONa} - \text{CH}_3\text{COOK}$, has a transition point P at 197° and 52.5% potassium acetate, 18.5% sodium caproate and 29.0% sodium acetate.

For an accurate determination of the temperatures at the compositions of the ternary invariant points, the crystallization lines were projected on the side $\text{CH}_3\text{COONa} - \text{CH}_3\text{COOK}$ (Fig. 7).

A comparison of the data obtained with the results of previous investigations of systems of sodium and potassium acetates with salts of other aliphatic acids [1] showed that as the number of carbon atoms increased in the aliphatic radical, the capacity of the system for complex formation increased. In the system $\text{Na, K} \parallel \text{CH}_3\text{COO, C}_2\text{H}_5\text{COO}$ the equilibrium is displaced toward the most refractory components, namely sodium acetate and potassium propionate. The system is diagonal. The compounds formed in the binary systems have no effect on the direction of the exchange reaction. In the systems $\text{Na, K} \parallel \text{CH}_3\text{COO, C}_3\text{H}_7\text{COO}$ and $\text{Na, K} \parallel \text{CH}_3\text{COO, C}_5\text{H}_{11}\text{COO}$ complex formation predominates over exchange decomposition reactions. These systems are adlagonal of the zonal type. The fraction of the area belonging to complex compounds first increases with an increase in the number of carbon atoms and then decreases again.

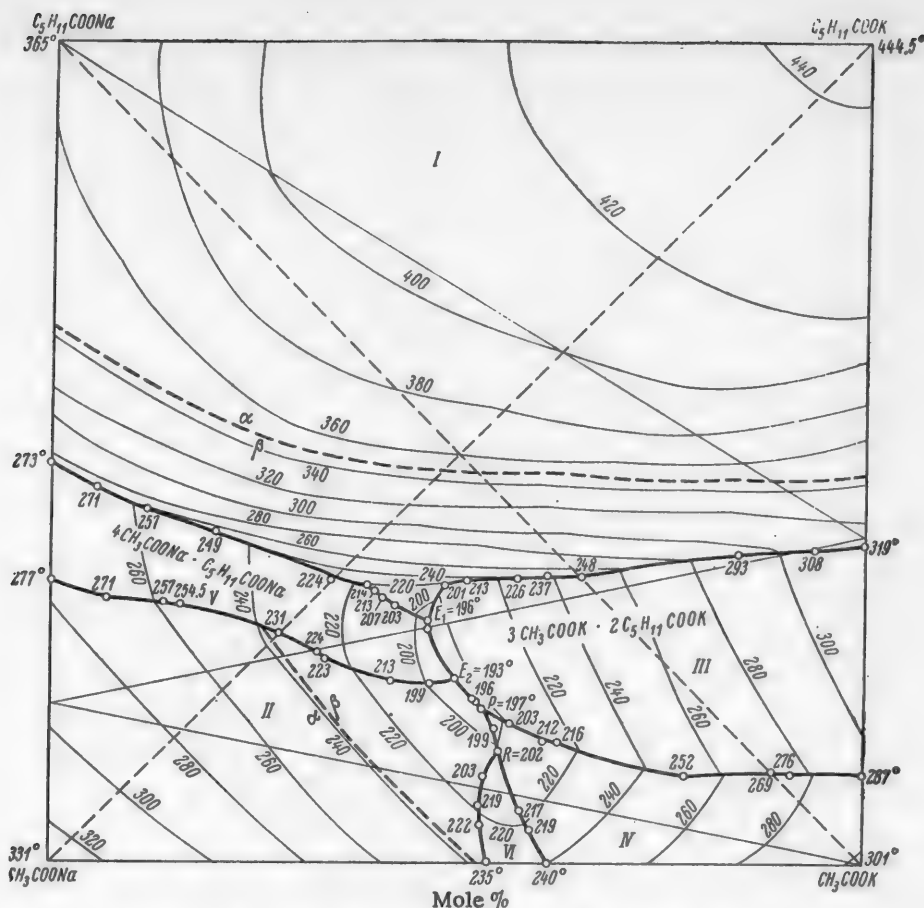


Fig. 6. Projection of the three-dimensional diagram of the ternary reciprocal system Na, K || CH_3COO , $\text{C}_6\text{H}_{11}\text{COO}$ on the composition square.

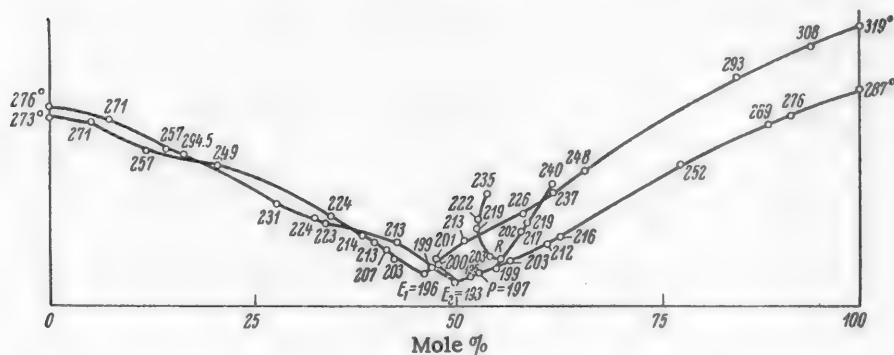


Fig. 7. Projection of cocrystallization lines on the side $\text{CH}_3\text{COONa}-\text{CH}_3\text{COOK}$.

SUMMARY

1. The ternary reciprocal system of sodium and potassium acetate and caproates was investigated for the first time.
2. The existence of the following complex compounds was established on the liquidus surface of the system: $3\text{CH}_3\text{COOK} \cdot 2\text{C}_6\text{H}_{11}\text{COOK}$, $4\text{CH}_3\text{COONa} \cdot \text{C}_6\text{H}_{11}\text{COONa}$ and $3\text{CH}_3\text{COOK} \cdot 2\text{CH}_3\text{COONa}$. Together these three fields occupy 17.3% of the total liquidus surface of the system.

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PHYSICOCHEMICAL STUDY OF SYSTEMS WITH DIPHENYLAMINE. I

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The capacity of diphenylamine to form molecular compounds with various organic materials, including acids, is at present of theoretical and practical interest as diphenylamine and its derivatives are used in various fields of the national economy.

It was established by physicochemical methods that diphenylamine undergoes acid-base reactions only with strong organic acids such as trichloroacetic, oxalic and succinic [1, 2]. An exception to this is the diphenylamine-lauric acid system, which was shown to form an equimolecular compound by O. A. Osipov and N. A. Trifonov [1].

As the systems of diphenylamine with organic acids were mostly studied through the melting point, we decided to study a series of systems using other methods in order to be able to elucidate the character of the reaction of diphenylamine with various substances in the liquid phase. To obtain the most complete picture possible of the interaction of the components, we studied the systems through viscosity, density, electrical conductivity and melting point.

TABLE 1

Viscosity and Density of the Formic Acid-Diphenylamine System (in dichloroethane)

Diphenyl- amine con- tent (in mole %)	Density		Viscosity		Specific electricocon- ductivity ($\times 10^5$)	
	50°	70°	50°	70°	50°	70°
0	1.1856	1.1660	0.629	0.487	0.69	0.81
20.70	1.1828	1.1582	0.863	0.677	1.95	1.68
30.56	—	1.1502	—	0.726	—	2.85
40.24	1.1708	1.1470	0.979	0.766	1.48	1.10
50.57	1.1629	1.1417	1.021	0.805	1.05	0.76
69.67	1.1544	1.1326	1.178	0.916	0.21	0.20
90.61	1.1417	1.1214	1.294	0.974	0.04	0.04
100	1.1395	1.1177	1.283	0.978	—	—

The viscosity was studied in a closed type of viscometer [3] in which the flow time of diphenylamine at 100° was 160 seconds. The density was measured in a 1 ml pycnometer. The electrical conductivity was measured in a closed vessel with platinum electrodes. An optical indicator with a three-cascade preamplifier of low frequency was used as a null instrument [4]. The measurements at 50-90° were made in a water thermostat and at 100-120°, in an oil one. The temperature was kept constant to $\pm 0.05^\circ$ with a mercury thermoregulator [5]. Thermal analysis was carried out by a visual polythermal method.

The substances used in the work were purified additionally by the usual methods and had the following melting points: diphenylamine, 53.5°, formic acid, 8.3° and acetic acid, 16.5°; the boiling point of caproic acid was 201.5-202° (734 mm) and that of acetic anhydride, 137.5° (725 mm).

TABLE 2

Viscosity and Density of the Acid-Diphenylamine System

Diphenyl- amine con- tent (in mole %)	Density			Viscosity		
	50°	70°	90°	50°	70°	90°
0	1.0162	0.9949	0.9719	0.818	0.621	0.472
10.31	1.0244	1.0040	0.9855	1.083	0.744	0.592
20.23	1.0302	1.0106	0.9899	1.242	0.898	0.650
40.39	1.0444	1.0255	1.0099	2.267	1.528	1.011
50.79	1.0500	1.0319	1.0154	2.799	1.712	1.144
61.13	1.0544	1.0374	1.0209	3.350	1.989	1.288
67.24	1.0530	1.0362	1.0210	3.714	2.153	1.385
78.95	1.0615	1.0438	1.0284	4.486	2.499	1.573
100	1.0635	1.0486	1.0304	5.993	3.152	1.854

TABLE 3

Electrical Conductivity of the Acetic Acid-Diphenylamine System

Diphenyl- amine con- tent (in mole %)	Specific electro- conductivity	
	50°	70°
0	9.84	—
11.88	3.34	5.38
19.96	2.15	2.91
47.09	0.32	0.63

The diphenylamine-formic acid system was studied in dichloroethane solution through its viscosity and density at 50 and 70° and its electrical conductivity at 70°. On investigating mixtures of pure components, it was established that in the range of diphenylamine concentrations from 5 to 95 mol.%, the viscosity increased noticeably with time and the mixture soon showed layer formation, which, according to literature data [6], is observed over the range of formic acid concentrations from 32 to 71 mol.%. Due to this layer formation, the system was studied in dichloroethane solution. Two solutions were prepared separately: one contained 30 mol. % of diphenylamine in dichloroethane and the other, 29.5 mol. % of formic acid.

As the freshly prepared mixtures showed an increase in viscosity with time, they were kept for 5 days at room temperature and the measurements then made. The mixtures formed layers at room temperature, but they were homogeneous at the temperature of the measurements. Only the mixture with 30 mol. % of diphenylamine was heterogeneous at 50°.

The results of the measurements are given in Table 1. The density isotherms were straight lines, while the viscosity isotherms were bent in toward the composition axis. The electroconductivity isotherm had a maximum at 30 mol. % of diphenylamine.

The diphenylamine-acetic acid system was studied through its viscosity, density and electroconductivity at 50, 70 and 90° and also through the melting point. The results of the measurements are given in Tables 2-4. The density isotherms were bent in toward the composition axis, while those of viscosity were slightly bent out. The electrical conductivity fell rapidly from acetic acid to diphenylamine.

Thermal analysis of the system gave a diagram with one eutectic with m. p. 11° and a diphenylamine content of 11 mol.%. These data differ somewhat from those reported by N. A. Trifonov [7].

The diphenylamine-caproic acid system was studied through viscosity and density at 50, 70 and 80°. The results of the measurements are given in Table 5. The density isotherms were slightly bent in toward the composition axis and those of viscosity were slightly bent out.

In the diphenylamine-acetic anhydride system the viscosity changed greatly with time. Therefore all the mixtures were first sealed in glass ampoules and heated for 20 hours on a boiling water bath. The mixtures after heating did not conduct a current and showed a tendency toward extreme supercooling.

The results of measuring the viscosity and density of the diphenylamine-acetic anhydride system at 50, 70 and 80° are given in Table 6. The viscosity and density isotherms passed through a maximum in the region of 60

TABLE 4

Melting Point of the Acetic Acid--Diphenylamine System

Diphenyl- amine con- tent (in mole %)	Melting point	
	of mixture	of eutectic
0	16.5°	—
8.97	12.5	11.7°
10.31	11.7	—
11.88	12.5	11.0
20.23	19.7	11.0
30.21	28.1	11.5
40.39	34.8	11.7
50.79	38.5	—
61.13	42.5	—
67.24	44.5	—
78.94	47.6	—
100	53.5	—

mol. % of diphenylamine. On cooling, the mixtures deposited crystals which melted at 103° after recrystallization from ligroine. A mixed melting point with acetodiphenylamine was not depressed, confirming the formation of acetodiphenylamine [8].

DISCUSSION OF RESULTS

Diphenylamine is an extremely weak base and therefore its capacity to form molecular compounds with acids will depend to a large extent on the strength of the latter. Our experimental data as well as those of other authors [2] show that acetic acid and weaker organic acids do not form molecular compounds with diphenylamine.

The diphenylamine-formic acid system is somewhat different from the rest. It is known from literature data that formic acid forms compounds with amines and some of these are readily converted into the corresponding formyl derivatives [9]. The data we obtained show that a reaction occurs in the diphenylamine-formic acid system to give formyldiphenylamine and not a molecular compound of the components. It is quite probable that com-

plex formation by diphenylamine and formic acid preceded the formation of formyldiphenylamine. The change in viscosity with time and also the layer formation indicate the formation of formyldiphenylamine. We obtained formyldiphenylamine by vacuum distillation of an equimolecular mixture of diphenylamine and formic acid which

TABLE 5

Viscosity and Density of the Caproic Acid-Diphenylamine System

Diphenyl- amine con- tent (in mole %)	Density			Viscosity		
	50°	70°	80°	50°	70°	80°
0	0.9014	0.8343	0.8760	1.762	1.300	1.163
21.11	0.9439	0.9275	0.9187	2.271	1.581	1.356
39.83	0.9765	0.9599	0.9519	2.789	1.874	1.571
59.72	1.0077	0.9913	0.9846	3.497	2.206	1.831
79.57	1.0383	1.0227	1.0146	4.496	2.723	2.160
100	1.0615	1.0486	1.0400	6.100	3.260	2.570

TABLE 6

Viscosity and Density of Acetic Anhydride-Diphenylamine System

Diphenyl- amine con- tent (in mole %)	Density			Viscosity		
	50°	70°	80°	50°	70°	80°
0	1.0430	1.0204	1.0015	0.633	0.529	0.477
3.01	1.0435	1.0211	1.0098	0.709	0.569	0.521
13.14	1.0460	1.0255	1.0214	0.853	0.683	0.632
35.00	1.0699	1.0518	1.0425	3.044	1.994	1.654
45.00	1.0775	1.0589	1.0498	5.827	3.390	2.629
55.00	1.0796	1.0618	1.0532	11.471	5.369	4.045
65.00	1.0759	1.0590	1.0516	11.599	5.368	4.045
75.00	1.0733	1.0573	1.0495	10.085	4.806	3.641
85.00	1.0697	1.0535	1.0449	8.141	4.134	3.209
95.00	1.0631	1.0486	1.0407	6.641	3.564	2.782
100	1.0615	1.0483	1.0400	6.105	3.265	2.580

had first been heated on a boiling water bath. After recrystallization from dilute alcohol, the formyldiphenylamine had m. p. 72.5°.

It is known that amines and anhydrides of dibasic acids give addition products with an equimolecular composition and, in particular, diphenylamine gives such compounds with maleic [10] and tetrachlorophthalic anhydrides [11]. An exchange reaction occurs in the diphenylamine-acetic anhydride system and as a result, acetodiphenylamine and acetic acid are formed even at 50°. Since acetic acid does not form molecular compounds with diphenylamine, acetic anhydride is used for preparing acetodiphenylamine [8, 12].

A study of the exchange reaction is very valuable for physicochemical analysis. In systems with exchange reactions studied previously, the viscosity maximum indicates the ratio of the substances reacting [13]. In the diphenylamine-acetic anhydride system, however, the viscosity maximum is displaced toward diphenylamine, which probably may be explained by incomplete reaction.

SUMMARY

1. Systems of diphenylamine with formic, acetic and caproic acids were studied through their viscosity and density, those with formic and acetic acids, through electrical conductivity and that with acetic acid, through melting point.
2. It was established that acetic and caproic acids do not form molecular compounds with diphenylamine.
3. It was shown that in the diphenylamine-formic acid system the physicochemical diagrams reflect the formation of formyldiphenylamine.
4. The diphenylamine-acetic anhydride system, in which an exchange reaction occurs, was studied through viscosity and density. It was established that the maximum on the viscosity isotherms is displaced from an equimolecular ratio of the components toward diphenylamine.

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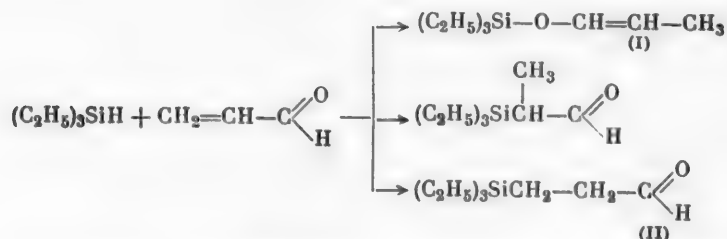
SYNTHESIS AND REACTIONS OF VINYL ETHERS OF SILANOLS

S. I. Sadykh-Zade and A. D. Petrov

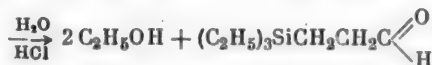
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We recently reported [1] the addition of triethylsilane to α, β -unsaturated aldehydes and ketones in the presence of H_2PtCl_6 . In this short communication we presented preliminary evidence of addition in the 1,4-position [and the $(C_2H_5)_3Si$ group to the oxygen], as a result of which, this reaction is a method of synthesizing silicon-containing vinyl ethers. In the present article we present more detailed evidence of the given order of addition and voluminous experimental material on the addition of triethylsilane and its analogs to many α, β -unsaturated aldehydes and ketones of various structures. The data obtained indicate that the yields of silicon-containing vinyl ethers vary over a wide range (from 11 to 93%), depending on the structure of the reaction components, and also that the reaction has a general character.

It can be assumed that the reaction proceeds according to the following equations:



The product to which structure (I) was assigned was hydrolyzed by dilute acid to form propionaldehyde (2,4-dinitrophenylhydrazone with m. p. 155°) and hexaethyldisiloxane. However, it was necessary to demonstrate that the isomeric compound (II) was incapable of this hydrolysis and differed from compound (I) in physical and chemical properties. Compound (II) could be obtained by the following reactions:



The physical and optical properties of these compounds were found to be different.

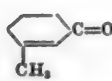
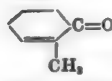

Compound (I) has b. p. 49-50° (6 mm), n_D^{20} 1.4320, d_4^{20} 0.8363. Raman spectrum: 298 (2), 450 (0), 543 (3), 580 (4 broad), 732 (0), 797 (2), 822 (1), 978 (4), 1014 (4), 1111 (0), 1232 (4), 1264 (4), 1307 (0), 1343 (2), 1393 (1), 1412 (3), 1462 (8 broad), 1667 (6), 2881 (10), 2909 (6), 2935 (2), 2955 (4). Compound (II) has b. p. 77-78° (5 mm), n_D^{20} 1.4472, d_4^{20} 0.8693. Raman spectrum: 166 (1), 257 (1 broad), 300 (3), 343 (0), 519 (2), 552 (7), 568 (7), 646 (1 broad), 746 (0), 763 (0), 880 (1), 979 (5), 1021 (5 broad), 1053 (1), 1105 (3).

Compound (II) was not hydrolyzed after being boiled with 6% H_2SO_4 for 3 hours and reacted with 2,4-dinitrophenylhydrazine to give a hydrazone with m. p. 105-106°. Rough experiments established that when one of the

TABLE 1

Reagents		Vinyl ethers obtained	
aldehydes	silanes	formula	
$\text{CH}_2=\text{CH}-\text{C}(=\text{O})\text{H}$	$(\text{C}_2\text{H}_5)_2\text{SiH}$ $(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiH}$ $[(\text{C}_2\text{H}_5)_2\text{SiH}]_2\text{O}$	$(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCH}_3$ $(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCH}_3$ $[(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCH}_3]_2\text{O}$	
$\text{CH}_3-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{H}$	$(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5)_2\text{SiH}$ $(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5\text{CH}_2)_2\text{SiH}$ $(\text{C}_2\text{H}_5)_3\text{SiH}$	$(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5)_2\text{SiOCH}=\text{CHCH}_3$ $(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5\text{CH}_2)_2\text{SiOCH}=\text{CHCH}_3$ $(\text{C}_2\text{H}_5)_3\text{SiOCH}=\text{CHCH}_2\text{CH}_3$	
$\text{C}_6\text{H}_5\text{CH}=\text{CH}-\text{C}(=\text{O})\text{H}$	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCH}_2\text{C}_6\text{H}_5$	
$\text{C}_6\text{H}_5\text{CH}=\text{CH}-\text{C}(=\text{O})\text{H}$	$(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCH}_2\text{CH}_2\text{C}_6\text{H}_5$	
$\text{CH}_3\text{C}(\text{CH}_3)=\text{CHCH}_2\text{CH}_2\text{C}(\text{CH}_3)=\text{CHC}(=\text{O})\text{H}$	$(\text{C}_2\text{H}_5)_2\text{SiH}$ $(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCHC}(\text{CH}_3)_2\text{H}_{11}$ $(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiOCH}=\text{CHCHC}(\text{CH}_3)_2\text{H}_{11}$	

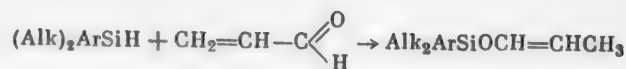
TABLE 2

Reagents		Vinyl ethers obtained	
ketones	silanes	formula	name
$\text{CH}_3-\text{CH}=\text{CO}-\text{CH}_3$	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}_3$	α, β -Dimethylvinyl-oxyltriethylsilane
$\text{CH}_3-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}-\text{CH}_3$	$\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}(\text{CH}_3)_2$	α -Methyl- β -isopropylvinyl-oxyltriethylsilane
	$(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{CH}_3)(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}(\text{CH}_3)_2$	α -Methyl- β -isopropylvinyl-oxymethyldiethylsilane
	$[(\text{C}_2\text{H}_5)_2\text{SiH}]_2\text{O}$	$[(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}(\text{CH}_3)_2]_2\text{O}$	Bis- α -methyl- β -isopropylvinyl-oxyltetraethylsiloxane
	$(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}(\text{CH}_3)_2$	α -Methyl- β -isopropylvinyl-oxylphenyldiphenylsilane
	$(\text{C}_2\text{H}_5)(\text{CH}_3\text{O})_2\text{SiH}$	$(\text{C}_2\text{H}_5)(\text{CH}_3\text{O})_2\text{SiOC}(\text{CH}_3)=\text{CHCH}(\text{CH}_3)_2$	α -Methyl- β -isopropylvinyl-oxylmethoxydimethoxysilane
$(\text{CH}_3)_2\text{C}=\text{CHCOCH}=\text{C}(\text{CH}_3)_2$	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}(\text{CH}_3)_2$	α -Isobutenyl- β -isopropylvinyl-oxyltriethylsilane
	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiO}-\text{C}_6\text{H}_9$	3-Methylcyclohexenyl-1-oxyltriethylsilane
	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiO}-\text{C}_6\text{H}_9$	2-Methylcyclohexenyl-1-oxyltriethylsilane
$\text{C}_6\text{H}_5-\text{CH}=\text{CH}-\text{CO}-\text{CH}_3$	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}_2\text{C}_6\text{H}_5$	β -Benzyl- α -methylvinyl-oxyltriethylsilane
	$(\text{C}_2\text{H}_5)_2\text{SiH}$	$(\text{C}_2\text{H}_5)_2\text{SiOC}(\text{CH}_3)=\text{CHCH}_2-\text{C}_4\text{H}_3\text{O}$	β -Furyl- α -methylvinyl-oxyltriethylsilane

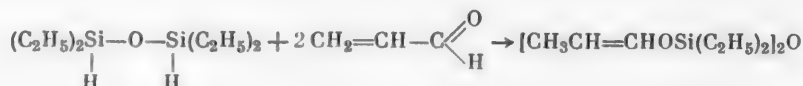
name	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Yield (in %)	Found (%)			Empirical formula	Calculated %		
					C	H	Si		C	H	Si
β -Methylvinyl-oxytriethylsilane	49—50° (6)	1.4320	0.8303	62.7	—	—	—	—	—	—	—
β -Methylvinyl-oxy-methyldiethylsilane	49.0 (15)	1.4248	0.8241	70.0	—	—	—	—	—	—	—
Bis- β -methylvinyl-tetraethyldisiloxane	94—96 (2)	1.4352	0.9154	60.0	55.73	10.17	18.52	$C_{14}H_{30}O_3Si_2$	55.56	9.99	18.56
β -Methylvinyl-oxy-ethylphenylsilane	131—133 (1)	1.5571	1.0272	35.0	75.55, 75.45	7.81, 7.64	10.87, 10.42	$C_{17}H_{20}OSi$	76.11	7.48	10.42
β -Methylvinyl-oxy-ethylphenylsilane	152—153 (1)	1.5509	1.01270	60.0	76.43, 76.25	8.10, 8.05	9.80, 9.91	$C_{19}H_{24}OSi$	77.03	8.11	9.46
β -Ethylvinyl-oxytriethylsilane	48 (2)	1.4330	0.8318	75.0	64.50, 64.76	11.95, 12.01	14.69, 14.85	$C_{10}H_{22}OSi$	64.51	11.82	15.05
β -Benzylvinyl-oxytriethylsilane	119—120 (2)	1.4060	0.9267	70.0	72.41, 72.58	9.96, 9.79	11.11, 11.18	$C_{15}H_{24}OSi$	72.52	9.71	11.30
β -Benzylvinyl-oxy-methyldiethylsilane	103—104 (2)	1.4050	0.9278	75	71.56, 71.80	9.46, 9.51	12.17, 12.02	$C_{14}H_{22}OSi$	71.80	9.40	11.97
2,6-Dimethyl-hexene-2-vinyl-oxytriethylsilane	103—103.5	1.4560	0.8481	58	71.85, 71.51	12.13, 11.89	10.25, 10.17	$C_{16}H_{30}OSi$	71.64	11.94	10.45
2,6-Dimethyl-hexene-2-vinyl-oxy-methyldiethylsilane	88—89 (1)	1.4530	0.8456	55	70.43, 70.46	11.62, 11.61	11.17, 10.83	$C_{15}H_{28}OSi$	70.79	11.88	11.42

Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Yield (in %)	Found (%)			Empirical formula	Calculated (%)		
				C	H	Si		C	H	Si
55—57° (3)	1.4380	0.8477	—	—	—	—	—	—	—	—
71—72 (4)	1.4375	0.8333	93.0	67.09, 67.17	12.23, 12.36	12.41, 13.06	$C_{12}H_{20}OSi$	67.29	12.15	13.08
65—65.5 (6)	1.4300	0.8220	90.0	65.86, 66.17	12.34, 12.21	13.84, 13.71	$C_{11}H_{21}OSi$	65.92	12.05	14.01
141—142 (3)	1.4442	0.9004	37.6	62.00, 61.98	10.93, 10.95	14.34, 14.65	$C_{20}H_{42}O_3Si_2$	62.11	10.95	14.52
139—141 (1)	1.5390	0.9970	11.0	77.25, 77.35	8.31, 8.57	8.85, 8.72	$C_{20}H_{38}OSi$	77.35	8.44	9.04
59—60 (4)	1.4210	0.9224	35.0	54.37, 54.42	10.87, 10.65	12.45, 12.56	$C_{10}H_{22}O_3Si$	55.90	10.20	12.85
86—87.5 (2)	1.4543	0.8588	42.0	—	—	11.35, 10.98	$C_{15}H_{30}OSi$	—	—	11.43
82—83	1.4568	0.8823	80.0	67.05, 68.13	11.58, 11.40	12.92, 13.53	$C_{12}H_{24}OSi$	67.05	11.39	13.22
82—83 (2)	1.4550	0.8807	71.13	68.09, 68.12	11.59, 11.57	12.93, 12.99	$C_{12}H_{24}OSi$	67.85	11.39	13.22
134—135 (3)	1.4981	0.9322	77	—	—	—	—	—	—	—
123—124 (4)	1.4752	0.9488	38	—	—	—	—	—	—	—

alkyl radicals in the trialkylsilanes was replaced by aryl, the yields of the corresponding vinyl ethers decreased sharply.

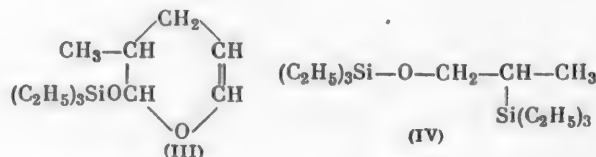


The addition of unsaturated aldehydes (and ketones) to tetraalkyldisiloxanes formed divinyl ethers by the reaction



EXPERIMENTAL

The reaction conditions have been described previously on the example of $(\text{C}_2\text{H}_5)_3\text{SiH}$ and acrylaldehyde [1]. Repeating the reaction made it possible to distill considerable amounts of reaction products and identify side products: the product from the addition of acrylaldehyde to β -methylvinylxytriethylsilane was evidently the cyclic acetal (III) and the product of the addition of a second molecule of triethylsilane to the vinyl ether was the unsaturated silicon-containing ether (IV).



Vacuum distillation of 260 g of products yielded:

- a) 160 g (62%) of the 1st fraction with b. p. 49-50° (6 mm), which was β -methylvinylxytriethylsilane; b) 30 g of the 2nd fraction with b. p. 91-92° (5 mm), n_D^{20} 1.4370, d_4^{20} 0.8570, which was hexaethyldisiloxane; c) 8 g of the 3rd fraction with b. p. 100-101° (5 mm), n_D^{20} 1.4500, d_4^{20} 0.9147.

Found %: C 62.02; H 10.79; Si 12.41. $\text{C}_{12}\text{H}_{24}\text{O}_2\text{Si}$. Calculated %: C 62.09; H 10.56; Si 12.29.

d) 9 g of the 4th fraction with b. p. 128-129° (4 mm), n_D^{20} 1.4550, d_4^{20} 0.9049.

Found %: C 62.38; H 12.47; Si 19.01. $\text{C}_{18}\text{H}_{36}\text{OSi}_2$. Calculated %: C 62.44; H 12.55; Si 19.46.

Hydrolysis of β -methylvinylxytriethylsilane. Into a flask fitted with a reflux condenser and a stirrer were placed 50 ml of H_2O , 2 ml of H_2SO_4 and 51.6 g of β -methylvinylxytriethylsilane. The mixture was heated to 80-90° for 2 hours. The reaction product (47 g) was distilled at atmospheric pressure.

1st fraction, 14 g, b.p. 49°, n_D^{20} 1.3640, d_4^{20} 0.8058. According to data in [2], propionaldehyde has b.p. 49.5°, n_D^{20} 1.3635, d_4^{20} 0.8066; reaction with 2,4-dinitrophenylhydrazine gave a hydrazone with mp. 154-155° (the starting β -methylvinylxytriethylsilane also gave the same hydrazone). According to data in [3], the 2,4-dinitrophenylhydrazone of propionaldehyde has m.p. 155°.

2nd fraction, 9 g, b. p. 155-156°, d_4^{20} 0.8650. The following constants are given [4] for triethylsilanol: b.p. 153-154°, d_4^{20} 0.8647.

3rd fraction, 16 g, b. p. 232-234°, n_D^{20} 1.4355, d_4^{20} 0.8575. The following constants have been reported [1] for hexaethyldisiloxane: b. p. 233°, n_D^{20} 1.4340, d_4^{20} 0.8590.

γ -Diethoxypropyltriethylsilane and γ -triethylsilylpropionaldehyde. With stirring, 52 g of acrolein acetal (b. p. 122°) was added at 20° to 46.4 g of triethylsilane and 0.3 ml of a 1 N solution of chloroplatinic acid in isopropyl alcohol. The temperature rose spontaneously to 35°. The reaction was completed by heating to 160°. After removal of the unreacted starting materials by distillation, the residue (86 g) was distilled at 3 mm. The γ -diethoxypropyltriethylsilane isolated (76 g) had b. p. 97-98°, n_D^{20} 1.4370, d_4^{20} 0.8640.

72 g of γ -diethoxypropyltriethylsilane was introduced with stirring into a flask containing 100 ml of water and 5 ml of HCl and the mixture was heated for 1 hour. The organic layer was separated, washed with 3% sodium carbonate solution and then with water and dried over Na_2SO_4 . Distillation at 5 mm yielded 40 g of γ -triethylsilylpropionaldehyde. The mobile liquid had a pleasant smell.

B. p. 77-78°, n_D^{20} 1.4472, d_4^{20} 0.8693.

Found %: C 62.30; H 11.49; Si 15.74. $\text{C}_9\text{H}_{20}\text{OSi}$. Calculated %: C 62.77; H 11.63; Si 16.29.

Reaction with 2,4-dinitrophenylhydrazine gave a hydrazone with m. p. 105-106°.

Found %: N 15.49; $\text{C}_{15}\text{H}_{24}\text{O}_4\text{N}_4\text{Si}$. Calculated %: N 15.87.

Table 1 gives the products from the addition of triethylsilane and its analogs to α,β -unsaturated aldehydes and Table 2 gives the products of addition to α,β -unsaturated ketones (addition to ketones occurred under the same conditions as the addition to aldehydes). It is interesting to note that distillation of β -methylvinylxytriethylsilane that had been stored for 3 months yielded its dimer:

B. p. 116-118° (3 mm), n_D^{20} 1.4440, d_4^{20} 0.8828.

Found %: C 62.51; H 11.68; Si 15.95. $\text{C}_{18}\text{H}_{40}\text{O}_2\text{Si}_2$. Calculated %: C 62.79; H 11.62; Si 16.28.

SUMMARY

1. The addition of triethylsilane to acrylaldehyde yielded for the first time β -methylvinylxytriethylsilane and the addition of triethylsilane to acrylaldehyde acetal (with subsequent hydrolysis) gave the isomeric γ -triethylsilylpropionaldehyde.

2. It was shown that the synthesis of silicon-containing vinyl ethers is a general one and was applied to α,β -unsaturated aldehydes and ketones of various molecular weights and structures. However, the yield of products from addition in the 1,4-position changed over a wide range, depending on both the structure of the aldehydes (ketones) and the alkyl (aryl) silanes.

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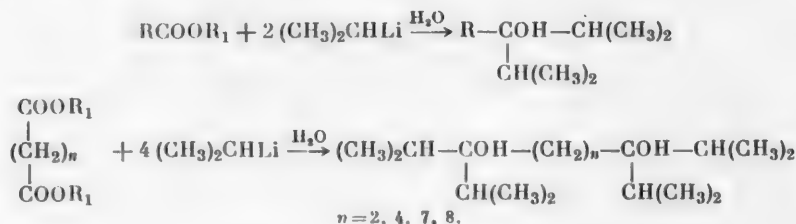
INTERACTION OF ISOPROPYLLITHIUM WITH ESTERS

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In a series of works [1] it was shown that an isopropylmagnesium halide reacts anomalously with esters of monobasic and dibasic acids and this leads to the formation of ketones, secondary alcohols and condensation products of two molecules of the original esters. No tertiary alcohols or ditertiary glycols are formed in this reaction. For example, the reaction of $\text{iso-C}_3\text{H}_7\text{MgCl}$ with ethyl caprylate gives a mixture of diheptyl ketone and heptyl isopropyl ketone [1]. The reactions of esters with *tert*-butylmagnesium halides proceed analogously. However, as we recently established [2], the replacement of *tert*-butylMgX by *tert*-butyllithium almost completely eliminates the formation of these anomalous products and as a result of the reaction, the corresponding tertiary alcohols and glycols are formed.

In the present investigation it was shown that the replacement of $\text{iso-C}_3\text{H}_7\text{MgX}$ by $\text{iso-C}_3\text{H}_7\text{Li}$ also leads to the formation of normal reaction products, namely, tertiary alcohols and ditertiary glycols, formed by the scheme presented below, and in even higher yields in this case.



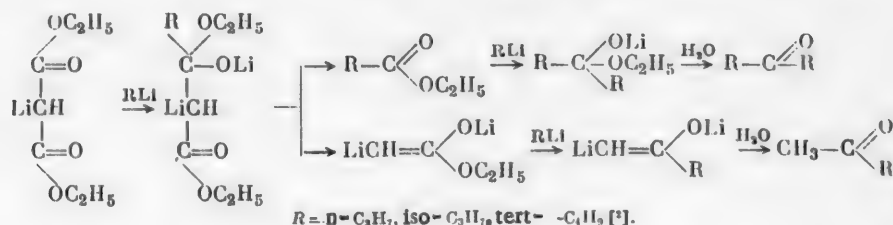
Thus, the condensation of $\text{iso-C}_3\text{H}_7\text{Li}$ with methyl caproate gave diisopropyl-*n*-amylcarbinol in 81% yield. Then ditertiary glycols were obtained in 50-80% yields from the dimethyl esters of adipic, azelaic and sebacic acids. 1,1,4,4-Tetraisopropylbutanediol-1,4 was formed from succinic ester in only 3% yield, while this ester did not form any glycol at all in a reaction with *tert*- $\text{C}_4\text{H}_9\text{Li}$. The condensation of $\text{iso-C}_3\text{H}_7\text{Li}$ with diethyloxalate did not even go to completion; we obtained a 60% yield of the keto alcohol 2,5-dimethyl-4-isopropyl-3-ketohexanol-4, which did not condense further with $\text{iso-C}_3\text{H}_7\text{Li}$. It is probable that an induction effect also plays a part in this reaction in addition to steric hindrance. The keto alcoholate $\text{iso-C}_3\text{H}_7-\text{C}-\text{C}(\text{iso-C}_3\text{H}_7)_2$ formed in the first

$$\begin{array}{c} \parallel \quad | \\ \text{O} \quad \text{OLi} \end{array}$$

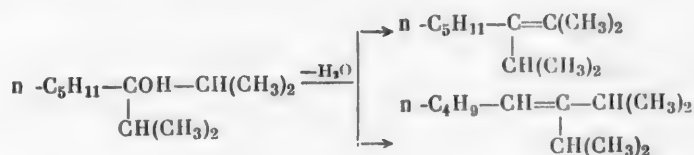
stage of the reaction contains a lithium atom, which decreases the negative charge of the oxygen atom of the adjacent carbonyl group and this decreases its reactivity.

As follows from literature data, the behavior of malonic ester in reactions with Grignard reagents is extremely varied. Thus, $\text{C}_6\text{H}_5\text{MgBr}$ [3] and $n\text{-C}_{10}\text{H}_{21}\text{MgBr}$ [4] react with this ester to form glycols, while $\text{iso-C}_3\text{H}_7\text{MgCl}$ [5] and CH_3MgI [6] produce only enolization of malonic ester and are themselves converted into C_3H_8 and CH_4 . In the present investigation we showed that $n\text{-C}_3\text{H}_7\text{MgBr}$ also reacts with malonic ester to produce enolization, while $\text{iso-C}_3\text{H}_7\text{Li}$ and $n\text{-C}_3\text{H}_7\text{Li}$ react with it differently. Besides liberation of the saturated hydrocarbon, we also observed the formation of methyl isopropyl ketone and diisopropyl ketone and in the case of $n\text{-C}_3\text{H}_7\text{Li}$, methyl propyl ketone

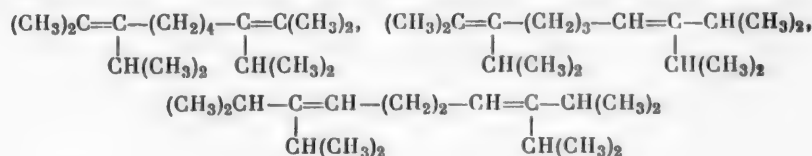
and dipropyl ketone. Apparently, the first stage of the reaction of malonic ester with organomagnesium or lithium compounds consists of replacement of a hydrogen atom of the methylene group by MgX or Li and this sharply lowers the reactivity of the carbonyl groups with respect to RMgX. On the other hand, having a greater reactivity, organolithium compounds react with these intermediate compounds by the following probable scheme:



The alcohol and glycols obtained in the present work were dehydrated over anhydrous CuSO_4 at 120–150° in vacuum. Ozonization of the olefins and diolefins formed showed that the dehydration proceeded without noticeable skeletal isomerization. For example, dehydration of 2-methyl-3-isopropyloctanol-3 yielded the olefins 2-methyl-3-isopropyloctene-2 and 2-methyl-3-isopropyloctene-3.



Dehydration of 1,1,6,6-tetraisopropylhexanediol-1,6 yielded a mixture of three olefins.



EXPERIMENTAL

Isopropyllithium was prepared by Bartlett's method [7]. Into a two-liter flask was introduced 28 g (4 g-atoms) of finely cut lithium and 700 ml of ether. The flask was placed in a bath with a cooling mixture (dry ice-acetone) and the contents cooled to -35°; then a solution of 158 g (2 mole) of iso-C₃H₇Cl in an equal volume of ether was added dropwise with the reaction mixture at -35 to -40°. When the whole of the chloride had been introduced, stirring was continued for a further half an hour. Solutions of 0.33 mole of the dimethyl esters of the dibasic acids (except in the case of condensation with methyl caproate, when 0.9 mole of ester was used) in 200 ml of ether were added over a period of 3 hours at -35 to -40° to the organolithium compound obtained and then the reaction mixture was stirred at the same temperature for a further hour. The unreacted lithium (1–3 g) was removed by filtration and the filtrate poured onto ice. After the usual processing and removal of the ether, the product was investigated.

1. Interaction of iso-C₃H₇Li with methyl caproate. Distillation of the reaction product on a column (40 cm long, 1 cm in diameter with glass rings 0.3 mm in diameter) yielded the following compounds:

a) Starting methyl caproate, 9.6 g; b) 2-methyloctanone, 3.8 g (9%), b. p. 93–94° (41 mm), n_D^{20} 1.4178, d_4^{20} 0.8144.

Found %: C 75.76, 75.78; H 12.72, 12.80. C₉H₁₈O. Calculated %: C 76.00, H 12.76.

Semicarbazone, m. p. 75–76.5°.

Found %: N 19.48, 19.56. C₁₀H₁₈ON₃. Calculated %: N 19.52. Literature data [8]: b. p. 182–184°, d_4^{20} 0.8341.

c) 2-Methyl-3-isopropyloctanol-3, 133 g (80%), b. p. 135-135.5° (41 mm), n_D^{20} 1.4483, d_4^{20} 0.8536.

Found %: C 77.40, 77.32; H 14.09, 14.15; OH 9.41. $C_{12}H_{26}O$. Calculated %: C 77.35; H 14.07; OH 9.16.

2. Interaction of iso- C_3H_7Li with diethyl oxalate. The main reaction product was the tertiary keto alcohol 2,5-dimethyl-4-isopropyl-3-ketohexanol-4 (46.5 g, 60.5%).

B. p. 118° (39 mm); m. p. 48.5-49° (from ligroine).

Found %: C 71.63, 71.45; H 11.80, 11.83; OH 9.05. M 182. $C_{11}H_{22}O_2$. Calculated %: C 70.92; H 11.90; OH 9.15. M 186.3.

The keto alcohol did not react with iso- C_3H_7Li .

3. Interaction of iso- C_3H_7Li with malonic ester. Distillation of the products on a column yielded the following compounds.

a) 2-methylbutanone-3, 9.3 g (30%), b. p. 93-95° (752 mm), n_D^{20} 1.3880, d_4^{20} 0.8011; melting point of 2,4-dinitrophenylhydrazone 120-121°.

Found %: N 21.30, 21.21. $C_9H_{12}O_4N_4$. Calculated %: N 21.08. Literature data [9]: b. p. 93-94° (752.5 mm), n_D^{20} 1.3879, d_4^{20} 0.815; melting point of 2,4-dinitrophenylhydrazone 118°.

b) 2,4-Dimethylheptanone-3, 13.7 g (36%), b. p. 122-124° (752 mm), n_D^{20} 1.4011, d_4^{20} 0.8005; melting point of 2,4-dinitrophenylhydrazone 96.5-97°.

Found %: N 19.20, 19.13. $C_{13}H_{16}O_4N_4$. Calculated %: N 19.04; melting point of 2,4-dinitrophenylhydrazone 94-98°.

4. Interaction of iso- C_3H_7Li with dimethyl succinate. After removal of the ether, the product was treated with an alcohol solution of NaOH to remove unreacted ester. Distillation gave 2 g (3%) of 2,7-dimethyl-3,6-diisopropyloctanediol-3,6.

B. p. 120° (4 mm), m. p. 79-80° (from ligroine).

Found %: C 74.79, 74.87; H 13.59, 13.47; OH 14.2. M 261. $C_{16}H_{34}O_2$. Calculated %: C 74.36; H 13.26; OH 13.2. M 258.4.

5. Interaction of iso- C_3H_7Li with dimethyl adipate. In addition to a small amount (9.6 g) of a liquid product, we obtained 87.2 g (80%) of 2,9-dimethyl-3,8-diisopropyldecanediol-3,8.

B. p. 169-173° (5 mm), m. p. 71-72° (from ligroine).

Found %: C 75.50, 75.62; H 13.24, 13.32; OH 11.9. M 281. $C_{18}H_{38}O_2$. Calculated %: C 75.46; H 13.37; OH 11.2. M 286.5.

6. Interaction of iso- C_3H_7Li with dimethyl azelate led to the formation of 53 g (49%) of 2,12-dimethyl-3,11-diisopropyltridecanediol-3,11.

B. p. 195° (2 mm), n_D^{20} 1.4721, d_4^{20} 0.9233; m. p. 90°.

Found %: C 76.49, 76.57; H 13.85, 13.70; OH 10.0. $C_{21}H_{44}O_2$. Calculated %: C 76.77; H 13.50; OH 10.37.

7. Interaction of iso- C_3H_7Li with dimethyl sebacate gave 58 g (50%) of 2,13-dimethyl-3,12-diisopropyl-tetradecanediol-3,12.

B. p. 210° (2.3 mm), n_D^{20} 1.4722, d_4^{20} 0.9167; m. p. 53.5-55°.

Found %: C 77.01, 77.20; H 13.33, 13.37; OH 9.9. $C_{22}H_{46}O_2$. Calculated %: C 77.12; H 13.53; OH 9.95.

8. Interaction of n- C_3H_7MgBr with malonic ester. To the organomagnesium compound prepared from 73 g of magnesium and 380 g of n- C_3H_7Br was added a solution of 80 g of malonic ester in 200 ml of ether. During the addition of the ester, a gas was liberated which did not decolorize bromine water and condensed at -50°. The boiling point of the gas was about -40°. When the whole of the ester had been added, the reaction mixture was stirred for a further 10 hours. The product was decomposed and processed in the usual way. Distillation yielded 58 g (73%) of the original malonic ester with b. p. 195-199° (754 mm), n_D^{20} 1.4141, d_4^{20} 1.0561.

9. Interaction of $n\text{-C}_3\text{H}_7\text{Li}$ with malonic ester. The reaction was carried out at 35° . Apart from the liberation of a saturated gas, the following compounds were isolated.

a) Pentanone-2, 11.7 g (38%), b. p. $98\text{--}102^\circ$, n_D^{20} 1.3919; melting point of 2,4-dinitrophenylhydrazone 141° . According to the data in [11]: b. p. 102° , n_D^{20} 1.3895; melting point of 2,4-dinitrophenylhydrazone 141° .

b) Heptanone-4, 17 g (45%), b. p. $141\text{--}143^\circ$, n_D^{20} 1.4100; melting point of 2,4-dinitrophenylhydrazone 72.5° . According to data in [11]: b. p. 144° , n_D^{20} 1.4093; melting point of 2,4-dinitrophenylhydrazone 75° .

The alcohol and glycols were dehydrated by heating with anhydrous CuSO_4 at $120\text{--}150^\circ$ and a pressure of 150 mm for 30 minutes. The product was distilled over sodium. The average yield of dehydration products was 70%.

1. The dehydration product of 2-methyl-3-isopropyloctanol-3 was a fraction with b. p. $94\text{--}97^\circ$ (38 mm), n_D^{20} 1.4390–1.4409, d_4^{20} 0.7747.

Found %: C 85.60, 85.54; H 14.55, 14.48. $\text{C}_{12}\text{H}_{24}$. Calculated %: C 85.62; H 14.38.

2. The dehydration product of 2,9-dimethyl-3,8-diisopropyldecanediol-3,8 was a fraction with b. p. $118\text{--}122^\circ$ (3 mm), n_D^{20} 1.4628–1.4640, d_4^{20} 0.8317.

Found %: C 86.25, 86.20; H 13.58, 13.80. $\text{C}_{18}\text{H}_{34}$. Calculated %: C 86.34, H 13.66.

3. The dehydration product of 2,12-dimethyl-3,11-diisopropyltridecanediol-3,11 was a fraction with b. p. $154\text{--}159^\circ$ (3 mm), n_D^{20} 1.4630–1.4646, d_4^{20} 0.8242.

Found %: C 86.07, 86.16; H 13.83, 13.86. $\text{C}_{21}\text{H}_{40}$. Calculated %: C 86.22; H 13.78.

4. The dehydration product of 2,13-dimethyl-3,12-diisopropyltetradecanediol-3,12 was a fraction with b. p. $158\text{--}160^\circ$ (3 mm), n_D^{20} 1.4640–1.4657, d_4^{20} 0.8231.

Found %: C 86.12, 86.00; H 13.80, 13.87. $\text{C}_{22}\text{H}_{42}$. Calculated %: C 86.19, H 13.81.

Ozonization of the dehydration product of 2-methyl-3-isopropyloctanol-3. Ozone was passed through a solution of 12 g of olefin in 60 ml of chloroform at 0° .

The ozonide was decomposed by boiling for 1 hour with 10 ml of H_2O_2 and 20 ml of water. The aqueous layer was shown to contain acetone, which gave a 2,4-dinitrophenylhydrazone melting at $123\text{--}124^\circ$. The melting point of a mixed sample was $124\text{--}125^\circ$. According to data in [11], the melting point of the 2,4-dinitrophenylhydrazone is 126° . After removal of the chloroform, the organic layer was hydrolyzed. A silver salt was obtained from the aqueous solution after evaporation and neutralization.

Found %: Ag 50.98. $\text{C}_4\text{H}_7\text{COOAg}$. Calculated %: Ag 51.61.

The organic residue (7 g) was distilled on a column (10 cm). The following compounds were isolated:

a) 2,4-Dimethylpentanone-3, 2 g, b. p. $120\text{--}124^\circ$, n_D^{20} 1.4005; melting point of 2,4-dinitrophenylhydrazone $94\text{--}96^\circ$. According to data in [10]: b. p. $124\text{--}125^\circ$, n_D^{20} 1.4001; melting point of 2,4-dinitrophenylhydrazone $94\text{--}98^\circ$.

b) 2-Methyloctanone-3, 1.5 g, b. p. $175\text{--}183^\circ$, n_D^{20} 1.4181; melting point of semicarbazone $73\text{--}74.5^\circ$.

The dehydration product of 2,9-dimethyl-3,8-diisopropyldecanediol-3,8 was ozonized similarly and among the reaction products we identified acetone, diisopropyl ketone and 2,9-dimethyldecanedione-3,8.

B. p. 250° (750 mm), n_D^{20} 1.4519, d_4^{20} 0.9259, MR_D 57.75; Calc. 57.64.

Found %: C 72.26, 72.47; H 11.15, 11.06. $\text{C}_{12}\text{H}_{22}\text{O}_2$. Calculated %: C 72.68; H 11.18.

Hydrogenation of olefins and diolefins. The olefins and diolefins obtained by dehydration of the alcohols were hydrogenated in heptane over Raney Ni at 180° and an initial hydrogen pressure of 130 atm for 18 hours. As a result we obtained the following paraffinic hydrocarbons, which have not been described in the literature.

2-Methyl-3-isopropyloctane. B. p. $193\text{--}194^\circ$ (751 mm); solid p. -125° , n_D^{20} 1.4285, d_4^{20} 0.7665, MR_D 57.21; Calc. 57.31.

Found %: C 84.78, 84.69; H 15.30, 15.23. $\text{C}_{12}\text{H}_{26}$. Calculated %: C 84.61; H 15.39.

2,9-Dimethyl-3,8-diisopropyldecane. B. p. 142-144° (20 mm); solid. p. -89°, n_D^{20} 1.4440, d_4^{20} 0.8079, MR_D 83.32; Calc. 83.65.

Found %: C 84.87, 84.99; H 14.84, 14.91. $C_{18}H_{38}$. Calculated %: C 84.95; H 15.05.

2,12-Dimethyl-3,11-diisopropyltridecane. B. p. 203-205° (20 mm); solid. p. -86°, n_D^{20} 1.4472, d_4^{20} 0.8041, MR_D 98.57; Calc. 99.17.

Found %: C 85.13, 84.96; H 15.03, 15.00. $C_{21}H_{44}$. Calculated %: C 85.05; H 14.95.

2,13-Dimethyl-3,12-diisopropyltetradecane. B. p. 214-216° (20 mm); solid. p. -83°, n_D^{20} 1.4493, d_4^{20} 0.8073, MR_D 103.24, Calc. 103.79.

Found %: C 85.28, 85.17; H 14.94, 14.89. $C_{22}H_{46}$. Calculated %: C 85.07; H 14.93.

SUMMARY

1. It was established that in contrast to an isopropylmagnesium halide, isopropyllithium reacts with esters of monobasic and high-molecular dibasic acids (adipic, azelaic and sebacic) by the normal scheme to form tertiary alcohols and ditertiary glycols.

2. A series of tertiary alcohols and glycols obtained by the above method were dehydrated over $CuSO_4$ at 120-150° and as ozonization showed, the dehydration proceeded without isomerization. Hydrogenation of the olefins and diolefins yielded for the first time C_{12} - C_{22} paraffinic hydrocarbons, which had isopropyl side chains, relatively high specific gravities and low solidification points.

3. In the case of oxalic ester, the reaction also proceeded by the normal scheme but to the tertiary keto alcohol and not to the glycol. In the case of malonic ester, the reaction proceeded with decomposition of the keto alcohol and the formation of methyl isopropyl ketone and diisopropyl ketone.

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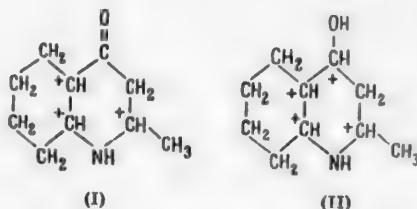
STEREOCHEMISTRY OF NITROGEN HETEROCYCLES

IV. STEREOISOMERISM OF 2-METHYL-4-HYDROXYDECAHYDROQUINOLINE

D. V. Sokolov, G. S. Litvinenko, and K. I. Khludneva

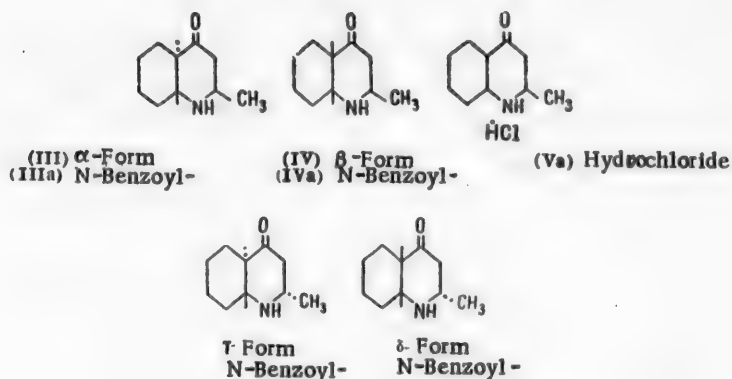
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In a previous article [1] we reported investigations of the stereoisomerism of 2-methyl-4-ketodecahydroquinoline (I) and described methods of preparing and separating the stereoisomeric ketones and also their properties.



The discovery of a simple isomerization of stable α - and γ -ketones into their unstable β - and δ -forms through the hydrochlorides made it possible to obtain all four theoretically predicted racemates of 2-methyl-4-ketodecahydroquinoline (scheme 1) and thus made these compounds accessible as starting materials for various syntheses of new stereoisomeric drugs.

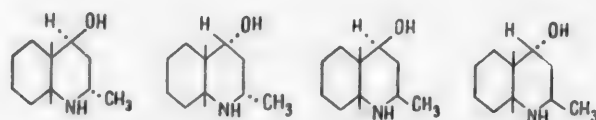
Scheme 1



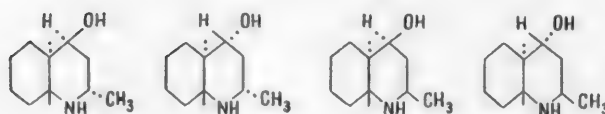
In view of the fact that an overwhelming majority of esters of 4-piperidols (cocaine and its piperidine analogs) have a high physiological activity, we decided to study in the first instance the stereoisomerism of 2-methyl-4-hydroxydecahydroquinoline (II) and to describe methods of preparing the stereoisomeric alcohols as starting materials for the preparation of anesthetics.

2-Methyl-4-hydroxydecahydroquinoline (II) has four asymmetric carbon atoms and therefore may exist in the form of eight isomer-racemates, whose steric structures may be represented by the following structural formulas (Scheme 2).

Scheme 2



Cis-series (with respect to ring coupling)

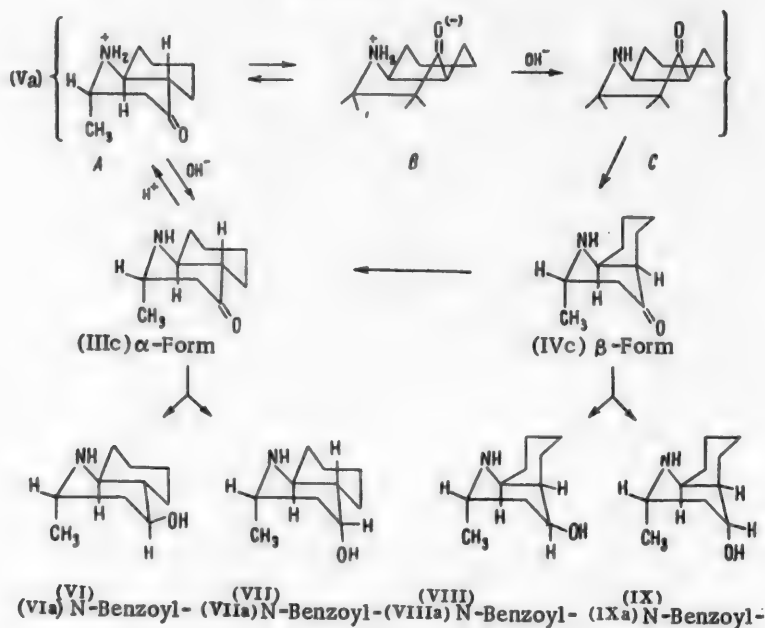


Trans-series (with respect to ring coupling)

In the present article we describe the stereoisomerism of the alcohols obtained by reduction and catalytic hydrogenation of α - and β -isomers of 2-methyl-4-ketodecahydroquinoline (III) and (IV), their benzoyl derivatives (IIIa) and (IVa) and the hydrochloride (V).

The α - and β -isomers of 2-methyl-4-ketodecahydroquinoline are connected by interconversions through the hydrochloride (Va) and in accordance with the principles of conformational analysis [1-3] have the following conformations (Scheme 3).

Scheme 3



The two pairs of epimeric alcohols (VI) and (VII), on the one hand, and (VIII) and (IX), on the other, must retain the conformations of the corresponding ketones (IIIb) and (IVb) and differ from each other (like the ketones) in the character of the ring coupling. As follows from Scheme 3, the first pair of alcohols are characterized by equatorial-equatorial coupling of the piperidine and cyclohexane rings, due to which they must belong to

the trans-series. The stereoisomeric alcohols (VIII) and (IX), which have equatorial-axial (e, a) coupling of the rings and a cis-disposition of the hydrogen atoms at C₉ and C₁₀, correspondingly belong to the cis-series. In all four alcohols, the methyl radical in the piperidine ring has an axial direction.

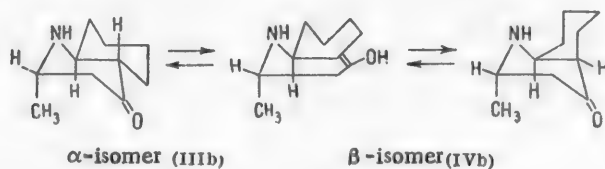
By using different methods of reducing the stereoisomeric ketones (IIIb) and (IVb) and their benzoyl derivatives (IIIa) and (IVa), we obtained all four theoretically predicted racemates of 2-methyl-4-hydroxydecahydroquinoline (VI)-(IX), corresponding in the structure of the carbon skeleton to the two original α - and β -ketones. The melting points of the alcohols and also their crystalline derivatives are given in Table 1.

TABLE 1

	Melting points of bases			
	133-134° (VI)	127-128° (VII)	188-189° (VIII)	131-132° (IX)
	Melting points of derivatives			
Hydrochloride	270-271°	196-197°	264-265°	190-193°
Picrate	177-178°	174-176°	223-224°	204-205°
N-Benzoyl derivative	138-139°	151-152°	210-211°	147-149°

Catalytic hydrogenation of the α -ketone (IIIb) (m. p. 63°) in the presence of Raney nickel formed a mixture of 2-methyl-4-hydroxydecahydroquinoline isomers, from which we isolated 10% of alcohol (VI) (m. p. 134°), 51% of (VII) (m. p. 128°) and 1.0% of (VIII) (m. p. 189°). Reduction of α -ketone (IIIb) with metallic sodium in anhydrous alcohol also led to the formation of a complex mixture of isomers; however, the yields of the given stereoisomeric alcohols in this case were reversed: 50% of (VI), 2% of (VII) and 20% of (VIII)*. The formation of alcohol (VIII) [4], which corresponds to the conformation of the unstable β -ketone (IVb), in both cases is probably explained by partial isomerization of the α -isomer (IIIb) into the β -isomer under the conditions of reduction and catalytic hydrogenation (Scheme 4) and also under the action of the basic properties of the amino group. We also cannot exclude the possibility of hydrogenation of the enol form, arising during the isomerization process and able to give alcohols with the conformations of both the cis- and the trans-series.

Scheme 4



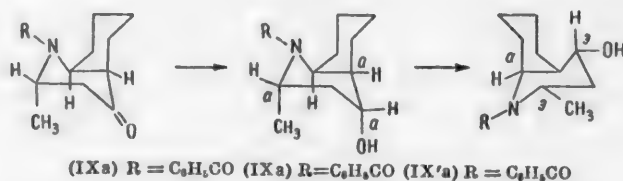
In the catalytic hydrogenation of the benzoyl derivative of the α -ketone (IIIa) (m. p. 138°), which lacks basic properties this isomerization did not occur and in this case we obtained only the two alcohols (VI) (7.5%) and (VII) (74%), corresponding structurally to the α -ketone (IIIb), and the alcohols (VIII) and (IX) which correspond structurally to the β -ketone (IVb) were not formed at all. The β -isomer (IVb) (m. p. 39°) was hardly hydrogenated at all under normal conditions in ligroine and a mixture of ligroine and alcohol with an Ni catalyst, but was slowly hydrogenated in water at 50°; it was then isomerized into the α -form (IIIb), forming the corresponding alcohols (VI) and (VII) in amounts of 10 and 59%, respectively. Alcohol (VIII), which corresponds structurally to the β -ketone (IVb), was isolated in a 5% yield with these hydrogenation conditions and we obtained about 1% of unpurified alcohol (IX) with m. p. 125-126° instead of 131-132°. The reduction of β -ketone (IVb) with metallic

* In all cases, the rest of the isomers to make up 100% remained as an unresolved mixture.

sodium in anhydrous alcohol was also accompanied by its isomerization into α -ketone (IIIb) and due to this, in addition to alcohol (VIII) (15%), we also obtained alcohols (VI) (33%) and (VII) (5%), which belong to the trans-series.

A study of the composition of the catalytic hydrogenation products of the benzoyl derivative of the β -ketone (IVa) (m. p. 132°) showed that in this case the two alcohols (VIII) (7.5%) and (IX) (71%) were formed as their N-benzoyl compounds (VIIIa) (m. p. 211°) and (IXa) (m. p. 149°) and also as the free bases with melting points of 189 and 132°, respectively (Scheme 3). The alcohols with the conformation of the α -ketone (IIIb) were not detected in the hydrogenation products, but from the latter we isolated an N-benzoyl derivative (10%) with m. p. 133° which was strongly depressed by a mixture with analogous derivatives of both the α - and β -ketones and also the alcohols (VI), (VII) and (IX), corresponding to them, and was consequently a new individual compound. We have not as yet established the steric structures of this substance; however, its formation is not unexpected. It is known that in the hydrogenation of the β -ketone (IVa), one of the two alcohols formed must have the hydroxyl group in the axial position (Scheme 5). Under the effect of the repulsive interactions of the three axial (aaa)

Scheme 5



substituents in the piperidine ring, producing strain in the molecule [5] and making it unstable, according to Hassel's rule [2], this alcohol (IXa) may isomerize into the more stable conformation of (IX'a), in which the hydroxyl group and the methyl radical will occupy equatorial positions. According to this hypothesis, it is possible that these alcohols are different conformations of the structure (IX).

Thus, while the stereoisomeric ketone-bases (IIIb) and (IVb) undergo interisomerization during reduction and both ketones simultaneously participate in the reduction reaction, in the catalytic hydrogenation of their benzoyl derivatives (IIIa) and (IVa) these isomerizations are not observed and alcohols are thus obtained whose structures strictly correspond to the configurations of the original α - and β -ketones.

The results of catalytic hydrogenation of the hydrochloride (Va) (m. p. 199°) in water in the presence of a nickel catalyst are interesting. Despite the fact that this salt is formed to an equal extent from both α - and β -ketones (IIIb) and (IVb), its hydrogenation yielded two alcohols, namely (VI) (5%) and (VII) (91%), corresponding in configuration only to the α -ketone (IIIb). This may be explained in the following way. As shown previously [1], the hydrochloride (Va) exists in aqueous solution in the form of the two conformations A and B, corresponding to the α - and β -ketones (III) and (IV), respectively. The conformation of the cation A in the form of two chairs, corresponding to the structure of the α -ketone, according to steric considerations is evidently hydrogenated more readily than the conformation of cation B in the form of two beds and due to this the equilibrium $A \rightleftharpoons B$ is completely displaced to the left in the hydrogenation. The yields of the alcohols obtained by reduction of the α - and β -ketones under various conditions are given in Table 2.

The stereoisomeric alcohols (VI) and (VIII), obtained in large amounts by reduction of the α - and β -ketones with sodium in alcohol and in smaller amounts by catalytic hydrogenation, should be assigned to the category of "stable" forms (Skita's rule) [6] and, according to the principles of conformational analysis, have the hydroxyl group in the equatorial position. The alcohols (VII) and (IX), obtained in opposite yields under the given conditions of reduction and hydrogenation (Table 2), must be correspondingly "labile" and their hydroxyl group must occupy an axial position. However, alcohol (IX) may have the twisted conformation (IXa) with an equatorial hydroxyl according to the considerations presented above (Scheme 5).

EXPERIMENTAL

α - and β - isomers of 2-methyl-4-ketodecahydroquinoline (IIIb) and (IVb) with the melting points 63 and 39° respectively, and also their benzoyl derivatives (IIIa) (m. p. 138°) and (IVa) (m. p. 132°) were prepared as

TABLE 2

Ketones	Reduction method	Solvent	Yields of alcohols (in %)			
			(VI) 134°	(VII) 128°	(VIII) 189°	(IX) 132°
α -Ketone (IIIb)	H ₂ /Ni	Alcohol	10	51	1	—
α -Ketone (IIIb)	Na + alcohol	The same	50	2	20	—
Benzamide (IIIa)	H ₂ /Ni	" "	7.5	74	—	—
β -Ketone (IVb)	H ₂ /Ni	Water, 50°	10	60	5	1
β -Ketone (IVb)	Na + alcohol	Alcohol	33	5	15	—
Benzamide (IVa)	H ₂ /Ni	The same	—	—	7.5	71
Hydrochloride (Va)	H ₂ /Ni	Water	5	91	—	—

described previously [1]. The Raney nickel catalyst was prepared in the following way [7]: 10 g of nickel-aluminum alloy was introduced in 2 g portions at 10 minute intervals into 100 ml of 30% sodium hydroxide solution. The catalyst was then heated to 70° on a water bath for 30 minutes, the alkali decanted and the remainder of it washed out with small portions of water (1 liter). The catalyst obtained was introduced into a hydrogenation flask. When the hydrogenation was performed in an organic solvent, the catalyst was also washed with alcohol and the required solvent. The catalyst was saturated with hydrogen before hydrogenation of the carbonyl compounds.

Hydrogenation of the α -isomer of 2-methyl-4-ketodecahydroquinoline (IIIb) over Raney nickel catalyst. 15.0 g of the α -isomer (IIIb) with m. p. 62-63° was hydrogenated in 70 ml of alcohol in the presence of nickel catalyst. After 12 hours the hydrogenation slowed considerably (1.2 liter of hydrogen was absorbed) and a new portion of catalyst was introduced into the flask. After 24 hours' shaking a total of 2.1 liters of hydrogen had been absorbed as compared with 2.2 liters required theoretically. The catalyst was removed by filtration, the alcohol evaporated to dryness under reduced pressure and the solid residue recrystallized from acetone. We obtained 7.7 g (50.7%) of the stereoisomer of 2-methyl-4-hydroxydecahydroquinoline (VII) with m. p. 127-128° as colorless platelets.

Found %: C 71.17, 71.11; H 11.40, 11.44; N 8.22, 8.29. C₁₈H₂₉ON. Calculated %: C 70.96; H 11.31; N 8.28.

The hydrochloride was obtained by neutralization of the base (VII) with a solution of dry hydrogen chloride in anhydrous alcohol. The fine, colorless needles had m. p. 196-197° (from anhydrous alcohol).

Found %: N 6.88, 6.77. C₁₈H₂₉ONCl. Calculated %: N 6.81.

The picrate was obtained by mixing alcohol solutions of equivalent amounts of the base and picric acid. The fine yellow needles had m. p. 174-176° (from dilute methyl alcohol).

Found %: C 48.23, 48.31; H 5.48, 5.32; N 14.44, 14.43. C₁₈H₂₂O₈N₄. Calculated %: C 48.24; H 5.57; N 14.06.

1-Benzoyl-2-methyl-4-hydroxydecahydroquinoline (VIIa) was obtained by benzylation of alcohol (VII) in the presence of alkali by the Schotten-Baumann reaction. The fine, colorless needles had m. p. 151-152° (from ligroine).

Found %: C 74.68, 74.86; H 8.37, 8.29; N 5.37, 5.18. C₁₇H₂₃O₂N. Calculated %: C 74.69; H 8.48; N 5.13.

The mixture of isomeric alcohols remaining after separation of alcohol (VII) and evaporation of the acetone was dissolved in anhydrous alcohol and neutralized with a solution of dry hydrogen chloride in anhydrous alcohol. On recrystallization from anhydrous alcohol, the precipitated crystals yielded 1.85 g (10%) of the hydrochloride of 2-methyl-4-hydroxydecahydroquinoline (VI) with m. p. 270-271°.

Found %: N 6.54, 6.51. C₁₈H₂₉ONCl. Calculated %: N 6.81.

The hydrochloride with m. p. 270-271° was dissolved in a small amount of water, decomposed with excess potassium carbonate and the liberated base extracted with chloroform and dried with solid potassium carbonate. Removal of the chloroform and recrystallization of the residue from acetone yielded 1.4 g of the second isomer of 2-methyl-4-hydroxydecahydroquinoline (VI) with m. p. 133-134° as fine, colorless needles.

Found %: C 71.01, 70.54; H 11.31, 11.04; N 8.27, 8.06. $C_{10}H_{19}ON$. Calculated %: C 70.96; H 11.31; N 8.28.

Neutralization of the base (VI) with an alcohol solution of hydrogen chloride formed the same hydrochloride with m. p. 270-271°, undepressed by admixture with the sample described.

The picrate formed attached yellow platelets with m. p. 177-178°.

Found %: C 48.05, 48.20; H 5.41, 5.51; N 14.46, 14.78. $C_{16}H_{22}O_8N_4$. Calculated %: C 48.24; H 5.57; N 14.06.

1-Benzoyl-2-methyl-4-hydroxydecahydroquinoline (VIa) was obtained by benzylation of isomer (VI) by the Schotten-Baumann method. The colorless platelets had m. p. 138-139° (from ligroine).

Found %: C 75.73, 75.87; H 8.53, 8.61; N 5.16, 5.33. $C_{17}H_{23}O_2N$. Calculated %: C 74.69; H 8.48; N 5.13.

The mixture of hydrochlorides remaining after separation of the hydrochloride of the isomeric alcohol (VI) with m. p. 270-271° was decomposed in an aqueous solution with potassium carbonate and the liberated base recrystallized from ether. We obtained 0.11 g of the third isomer of 2-methyl-4-hydroxydecahydroquinoline (VIII) with m. p. 188-189°, not depressed by admixture with an authentic sample (see below).

Reduction of the α -isomer of 2-methyl-4-ketodecahydroquinoline (IIIb) with metallic sodium in alcohol. 11 g of the α -isomer (IIIb) with m. p. 62-63° and 400 ml of anhydrous alcohol were placed in a flask with a reflux condenser and 30 g of metallic sodium introduced in small pieces into the solution with stirring over a period of one and a half hours. Toward the end of the reaction, the thick liquid was heated on a water bath until the sodium dissolved completely. The solution was acidified with 140 ml of concentrated hydrochloric acid in small portions with cooling in ice water and stirring. The precipitated sodium chloride was removed by filtration and washed with a large amount of alcohol. The alcohol solution was evaporated to dryness under reduced pressure; the residual mixture of hydrochlorides was dissolved in water, decomposed with excess potassium carbonate and the base extracted many times with ether. On standing overnight, the ether solution (400 ml) deposited 0.1 g of crystals with m. p. 188-189°. Evaporation of the solution and successive crystallizations yielded a further 1.6 g of the same substance. The crystals were combined and recrystallized from acetone. We obtained 1.6 g of the isomer of 2-methyl-4-hydroxydecahydroquinoline (VIII) with m. p. 188-189° as coarse, transparent needles.

Found %: C 71.64, 71.56; H 11.29, 11.45; N 8.14, 8.43. $C_{10}H_{19}ON$. Calculated %: C 70.96; H 11.31; N 8.28.

The hydrochloride was obtained by neutralization of the base (VIII) with a solution of dry hydrogen chloride in anhydrous alcohol with subsequent precipitation of the crystals with dry ether. The fine needles had m. p. 264-265°.

Found %: N 6.80, 6.46. $C_{10}H_{20}ONCl$. Calculated %: N 6.81.

The picrate was obtained as described above. The yellow needles had m. p. 223-224° (from anhydrous alcohol).

Found %: C 48.34, 48.41; H 5.45, 5.63; N 14.86, 14.68. $C_{16}H_{22}ON_4$. Calculated %: C 48.24; H 5.57; N 14.06.

1-Benzoyl-2-methyl-4-hydroxydecahydroquinoline (VIIIa) was obtained by the Schotten-Baumann method in the following way. 0.42 g of the isomer (VIII) with m. p. 188-189°, 0.53 g of benzoyl chloride and 1.8 ml of 10% sodium hydroxide solution were stirred with a glass rod until the smell of benzoyl chloride disappeared. After 3 hours the liquid was sucked off and the crystals washed with water and ether and recrystallized from anhydrous alcohol. We obtained 0.43 g of the benzoyl derivative of the isomeric alcohol (VIII) with m. p. 210-211° as very fine needles.

Found %: N 5.89, 5.79. $C_{17}H_{23}O_2N$. Calculated %: N 5.13.

The isomeric bases remaining after separation of alcohol (VIII) with m. p. 188-189° were converted into the hydrochlorides as described above and fractional crystallization of these from anhydrous alcohol yielded first 6.1 g of the hydrochloride of the isomeric alcohol (VI) with m. p. 270-271° and then 0.5 g of the hydrochloride of alcohol (VIII) with m. p. 264-265°, which did not depress the melting points of authentic samples. The remaining mixture of hydrochlorides was treated with potassium carbonate and the free bases isolated in the usual way and recrystallized from acetone. We obtained 0.5 g of alcohol (VIII), which was difficultly soluble in acetone and had m. p. 188-189°, and then 0.22 g of alcohol (VII), which was more readily soluble in acetone and had m. p. 127-128° and did not show depression with the sample obtained previously. The residue of the bases was again converted into the hydrochlorides, which were recrystallized from anhydrous alcohol to yield a further 0.7 g of the hydrochloride of alcohol (VI) with m. p. 270-271°. We thus obtained a total of 6.8 g (50.2%) of the hydrochloride of alcohol (VI) with m. p. 270-271°, 0.22 g (20%) of alcohol (VII) with m. p. 127-128° and 2.2 g (19.8%) of alcohol (VIII) with m. p. 188-189°. The residual unresolved mixture weighed 0.8 g (6.0%),

Hydrogenation of the hydrochloride of the α -isomer of 2-methyl-4-ketodecahydroquinoline (Va). 26.2 g of the hydrochloride (m. p. 199°) was hydrogenated in 120 ml of water in the presence of Raney nickel obtained from 10 g of nickel-aluminum alloy. The calculated amount of hydrogen (3.3 liters) was absorbed when the flask was shaken for 9 hours. The catalyst was removed and washed with 200 ml of hot water and then a considerable part of the water was removed in vacuum. The aqueous solution of hydrochlorides was treated with excess potassium carbonate and the base extracted with ether and dried with solid potassium carbonate. The ether solution was evaporated to dryness and the residual crystalline base recrystallized from acetone. We obtained 18.6 g of alcohol (VII) with m. p. 127-128°. The residue of isomers after complete evaporation of the acetone was converted into the hydrochlorides by the action of an alcohol solution of dry hydrogen chloride and recrystallization of these from anhydrous alcohol yielded 1.2 g of the hydrochloride of the isomeric alcohol (VI) with m. p. 270-271°. A second recrystallization of the residual mixture of alcohols in the form of the bases from acetone and then in the form of their hydrochlorides from anhydrous alcohol yielded in additional 1.1 g of alcohol (VII) with m. p. 127-128° and 0.2 g of the hydrochloride of alcohol (VI) with m. p. 270-271°. Thus, we isolated a total of 19.7 g (90.6%) of alcohol (VII) with m. p. 127-128° and 1.4 g (5.3%) of the hydrochloride of alcohol (VI) with m. p. 270-271° (melting point of alcohol-base, 133-134°). 0.5 g (2.3%) of the mixture remained unresolved.

Hydrogenation of the α -isomer of 1-benzoyl-2-methyl-4-ketodecahydroquinoline (IIIa). 15.0 g of the α -isomer (IIIa) with m. p. 138-139° was hydrogenated in 120 ml of alcohol (saturated solution) in the presence of a nickel catalyst. After 50 minutes shaking, 1.45 liters of hydrogen had been absorbed as compared with 1.47 liters calculated theoretically. A further 54.5 g of (IIIa) was hydrogenated under analogous conditions. The catalyst was removed and washed with alcohol. The combined hydrogenation products were fractionally crystallized first from alcohol and then from acetone. In this way we isolated 52.1 g (74%) of 1-benzoyl-2-methyl-4-hydroxydecahydroquinoline (VIIa) with m. p. 151-152° and 5.3 g (7.5%) of 1-benzoyl-2-methyl-4-hydroxydecahydroquinoline (VIa) with m. p. 138-139°, corresponding to alcohols (VII) (m. p. 128°) and (VI) (m. p. 134°), respectively, and not depressing the melting points of samples obtained previously. 13.6 g (16.1%) of an unresolved mixture of isomers remained.

Hydrogenation of the β -isomer of 2-methyl-4-ketodecahydroquinoline (IVb). 20.5 g of the β -isomer (IVb) with m. p. 38-39° was hydrogenated in 150 ml of water in the presence of a nickel catalyst in a glass flask with double walls, through which water at 50° was passed continuously. After 16 hours shaking, 3.1 liters of hydrogen had been absorbed as compared with 3.2 liters calculated theoretically. A further 20.1 g of the β -isomer (IVb) was hydrogenated under the same conditions. The catalyst was separated and washed with hot water. Subsequent evaporation of the aqueous filtrate yielded 17.2 g of crude alcohol (VII) with m. p. 124°. The residue was recrystallized from acetone with alternate introduction of seeds of (VII) and (VIII) and subsequent separation of the crystals formed (after 1.5 to 2 hours). When the melting point of (VII) fell to 120°, the bases were converted into the hydrochlorides, which were recrystallized from anhydrous alcohol to yield the hydrochloride of alcohol (VI). The isomers were then reconverted into the bases and recrystallized from diethyl ether. In this way, besides the isomers (VII) and (VIII), we isolated 0.86 g of unpurified alcohol (IX) with m. p. 124-127°, showing strong depression of melting point with (VI) and (VII). Alcohol (VI) was again isolated in the form of the hydrochloride. After recrystallizing the crude products, we obtained 24.5 g (59.5%) of the isomer of 2-methyl-4-hydroxydecahydroquinoline (VII) with m. p. 127-128° (from acetone), 2.0 g (4.9%) of isomer (VIII) with m. p. 188-189° (from acetone), 4.1 g (10%) of the hydrochloride of isomer (VI) with m. p. 270-271° (from anhydrous alcohol) and 0.42 g

(1%) of the unpurified isomer (IX) with m. p. 125-126°, melting at 98-103° when mixed with samples of (VI) (m. p. 134°) and (VII) (see below).

Reduction of the β -isomer of 2-methyl-4-hydroxydecahydroquinoline (IVb) with metallic sodium in alcohol. Reduction of 31.5 g of the β -isomer with m. p. 38-39° in 800 ml of alcohol with 60 g of metallic sodium and treatment of the reduction products were as described above. The colored hydrochlorides of the isomers, remaining after removal of the alcohol, were dissolved in water, washed with chloroform and decomposed with excess potassium carbonate and the liberated bases dried in chloroform solution. After 3 successive fractional recrystallizations of the mixture of isomer-bases from acetone [isolation of alcohols (VIII) and (VII)] and their hydrochlorides from anhydrous alcohol [isolation of hydrochloride (VI)], we obtained 12.9 g (33.3%) of the hydrochloride of isomer (VI) with m. p. 270-271°, 1.7 g (5.3%) of isomer (VII) with m. p. 127-128° and 4.9 g (15.4%) of isomer (VIII) with m. p. 188-189°, whose mixed melting points with authentic samples were not depressed. The residual mixture of isomers weighed 6.3 g (19.8%).

Hydrogenation of the β -isomer of 1-benzoyl-2-methyl-4-ketodecahydroquinoline (IVa) in the presence of a nickel catalyst. 6.3 g of the β -isomer (IVa) with m. p. 131-132° was hydrogenated in 130 ml of anhydrous alcohol in the presence of a nickel catalyst. Over a period of 3 hours shaking, 640 ml of hydrogen was absorbed as compared with 660 ml required theoretically. A further 10 g of (IVa) was hydrogenated under these conditions. The catalyst from both experiments was removed, washed with alcohol and the alcohol solution evaporated to dryness. The crystalline residue was boiled with three 200 ml portions of light ligroine (b. p. 60-70°) in a flask with a reflux condenser. Successive evaporations of the ligroine extracts yielded portions of an N-benzoyl derivative, which had m. p. 132-133° (1.3 g, 10%) after recrystallization from acetone and gave strong depression of melting point with the original ketone (IVa) (110-115°) and the alcohol (IVa) (106-110°).

Found %: C 73.77, 73.58; H 9.63, 9.36; N 4.95, 5.27. $C_{17}H_{23}O_2N$. Calculated %: C 70.96; H 11.31; N 5.13.

Fractional recrystallization of the ligroine-insoluble residue from alcohol yielded: a) 0.85 g (5.2%) of crystals with m. p. 210-211°, which were the N-benzoyl derivative (VIIIa) of alcohol (VIII) (m. p. 188-189°) and did not show depression of melting point with the sample described; b) 7.72 g (47.7%) of the N-benzoyl derivative (IXb) with m. p. 147-149° [m. p. of alcohol (IX) 131-132°, see below].

Found %: N 5.07, 5.19. $C_{17}H_{23}O_2N$. Calculated %: N 5.13

c) 5.7 g (35.2%) of a mixture of the benzoyl derivatives of alcohols (VIII) and (IX) with m. p. 143-147°.

Investigation of crystals with m. p. 143-147°. 5.7 g of the mixture of N-benzoyl derivatives of alcohols (VIII) and (IX) with m. p. 143-147° and 250 ml of dry dioxane, saturated with dry hydrogen chloride, were boiled under reflux on Wood's alloy for 17 hours. The dioxane solution was evaporated to dryness, the glassy residue treated with water and the precipitated crystals sucked off, washed with water and ether and dried in air. We obtained 0.84 g of the hydrochloride of the benzoate of alcohol (IX) with m. p. 250-251° (from anhydrous alcohol).

Found %: N 4.70, 4.61. $C_{17}H_{24}O_2NCl$. Calculated %: N 4.52.

The residual aqueous solution of hydrochlorides was washed with ether (to separate 1 g of starting material with m. p. 143-147°), treated with potassium carbonate and the free base extracted with ether and dried with sodium sulfate. Removal of the ether yielded 2.8 g of a semicrystalline mixture of bases, which was recrystallized from acetone to give: a) 0.25 g of alcohol (VIII) with m. p. 188-189°, undepressed by admixture with an authentic sample, and b) 1.34 g of unpurified alcohol (IX) with m. p. 125-127°, showing strong depression of melting point with alcohols (VI) and (VII) (25-30°). The residual bases after separation of alcohols (VIII) and (IX) were reconverted into the hydrochlorides, which were recrystallized from anhydrous alcohol to yield a further 0.34 g of the hydrochloride of the benzoate of alcohol (IX) with m. p. 250-251°. The total yield of this hydrochloride was 22.2%.

Benzoate of alcohol (IX). 0.9 g of the hydrochloride with m. p. 250-251° was shaken with a dilute aqueous solution of potassium carbonate in the presence of ether until the crystals had completely disintegrated (15 minutes). The base was exhaustively extracted with ether, dried with magnesium sulfate and recrystallized from ligroine (b.p. 40-50°) after removal of the solvent. We obtained 0.73 g (92%) of the benzoate of alcohol (IX) as nodules of clear crystals with m. p. 94-95°.

Found %: N 4.78, 4.79. $C_{17}H_{23}O_2N$. Calculated %: N 5.12.

The picrate was obtained in 95% yield by mixing equivalent amounts of the benzoate and picric acid in anhydrous alcohol. The yellow blocks had m. p. 233-234° (from anhydrous alcohol).

Found %: N 11.15, 11.20. $C_{23}H_{28}O_9N_4$. Calculated %: N 11.15.

2-Methyl-4-hydroxydecahydroquinoline (IX) with m. p. 131-132°. 0.45 g of the benzoate with m. p. 94-95° and 0.186 g of potassium hydroxide in 20 ml of anhydrous alcohol were boiled under reflux for 2 hours. The alcohol solution was diluted with 20 ml of water and the alcohol evaporated on a water bath. The residual aqueous solution was acidified with hydrochloric acid and extracted with ether. The ether extract was dried with sodium sulfate and the ether evaporated to give 0.195 g (97.5%) of benzoic acid with m. p. 120-121°, undepressed by admixture with an authentic sample. The aqueous solution was treated with excess solid potassium carbonate and the base extracted with ether, dried with potassium carbonate and recrystallized from acetone after removal of the ether. We obtained 0.267 g (95.6%) of 2-methyl-4-hydroxydecahydroquinoline (IX) as thick needles with m. p. 131-132°.

Found %: N 8.06, 8.50. $C_{10}H_{19}ON$. Calculated %: N 8.28.

The hydrochloride formed crystals with m. p. 191-193°.

Found %: N 6.65, 6.59. $C_{10}H_{20}ONCl$. Calculated %: N 6.81.

The picrate formed short yellow needles with m. p. 204-205° (from anhydrous alcohol).

Found %: N 13.92, 13.72. $C_{16}H_{22}O_8N_4$. Calculated %: 14.06.

The total yields of alcohols (VIII) and (IX) under the conditions of the hydrogenation of ketone (IVa) were 7.5 and 71%, respectively.

SUMMARY

1. The reduction of the α - and β -isomers of 2-methyl-4-ketodecahydroquinoline and other derivatives were studied and all four theoretically possible racemates of 2-methyl-4-hydroxydecahydroquinoline were obtained.

2. During catalytic hydrogenation in the presence of nickel and reduction with sodium in alcohol, the α - and β -ketones underwent interisomerization and formed a complex mixture of alcohols in each case. In the catalytic hydrogenation of the benzoyl derivatives of the α - and β -ketones, which lack basic properties, this isomerization did not occur and in this case the structure of the alcohols formed corresponded strictly to that of the starting ketones.

3. The structures of the stereoisomeric alcohols were examined in the light of the principles of conformational analysis. Alcohol (IX) may have the twisted conformation (IXa) with equatorial methyl and hydroxyl as a result of an excess of axial substituents in the molecule.

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INVESTIGATION IN THE FIELD OF 2,1,3-THIODIAZOLE CHEMISTRY

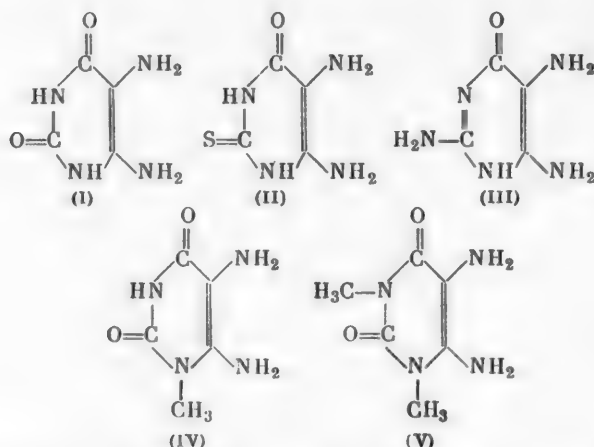
X. SYNTHESIS AND INVESTIGATION OF DERIVATIVES OF PYRIMIDINE-2,1,3-THIODIAZOLE

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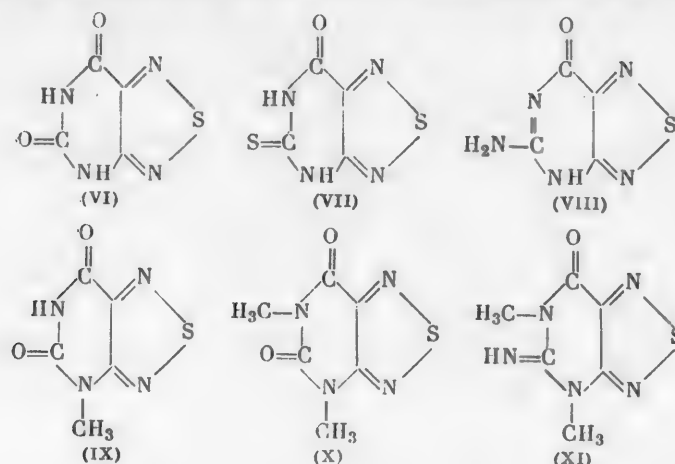
In developing an investigation in the field of 2,1,3-thiodiazole chemistry [1], we studied the synthesis of pyrimidine derivatives of this heterocycle. This was all the more interesting as according to opinions expressed in the literature [2], to show antitumor activity a molecule must contain at least two centers with different reactivities. In addition, we also considered the great importance of the pyrimidine ring in biological systems and the competing action of antimetabolites with metabolites [3].

It should be mentioned that pyrimidine-2,1,3-thiodiazole, which has a certain similarity to purines, has not been described in the literature and it seemed logical to extend to the synthesis of its derivatives the reaction of thionyl aniline with o-diamines of the aromatic and benzthiazole series, which we developed previously [1]. For this purpose we synthesized according to literature data some oxo, thio and amino derivatives of pyrimidine o-diamines and, in particular, 2,6-dioxo-4,5-diamino- (I) [4], 2-thio-6-oxo-4,5-diamino- (II) [5], 6-oxo-2,4,5-triamino- (III), 3-methyl-2,6-dioxo-4,5-diamino- (IV) [6] and 1,3-dioxo-4,5-diaminopyrimidines (V) [7], which were then cyclized with thionyl aniline to give relatively high yields (70-80%) of pyrimidine-2,1,3-thiodiazole derivatives. At the same time, it was found that under certain conditions pyrimidine o-diamines were able to react with thionyl aniline not only in the form of free bases but also as the salts and that the thiodiazole ring formed much more readily than the imidazole ring under identical conditions.

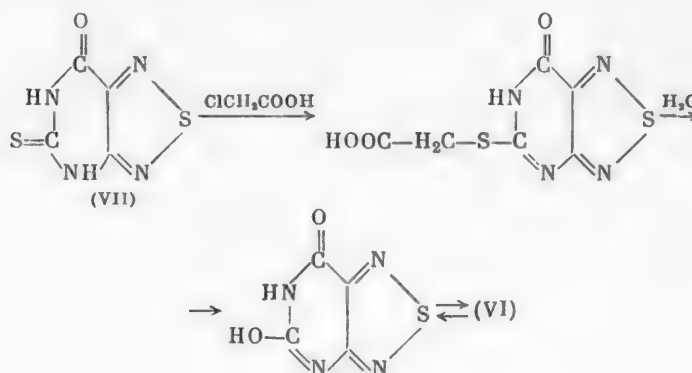


Condensations were carried out with both free bases and with their salts in the presence of potassium acetate. When acetic acid was used as a solvent, acetanilide was formed in addition to pyrimidine-2,1,3-thiodiazole derivatives. As regards purine derivatives, whose formation might be expected (in an acetic acid medium), these were not detected and this again demonstrates the high rate of closure of the thiodiazole ring.

During the synthesis, we synthesized for the first time 4,6-dioxypyrimidine-2,1,3-thiodiazole (VI), 4-oxo-6-thiopyrimidine-2,1,3-thiodiazole (VII), 4-oxo-6-aminopyrimidine-2,1,3-thiodiazole (VIII), 4,6-dioxo-7-methylpyrimidine-2,1,3-thiodiazole (IX) and 4,6-dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole (X).



For proving the structure of (VI), it was methylated with dimethyl sulfate in an alkaline medium to give (X), which was also synthesized by other methods, in particular, by the interaction of 1,3-dimethyl-2,6-dioxo-4,5-diaminopyrimidine (V) with thionyl aniline and also by methylation of the monomethyl derivative (IX). The product (VIII) was also methylated with dimethyl sulfate in an alkaline medium to give a substance which corresponded most closely in analysis to (XI). As we showed, (VII) did not undergo a reaction with dimethyl sulfate under the experimental conditions and in an attempt to methylate it with monochloroacetic acid, it was converted into (VI) as in the conversion of thiouracil into uracil [4]; the following scheme may be put forward to explain the reaction mechanism.



It should be noted that like guanine, compound (VIII) formed readily hydrolyzable salts, for example, the hydrochloride, and is similar in this respect to amines of the purine series. Diazotization of (VIII) formed (VI), which was converted into (X) when methylated with dimethyl sulfate as described above.

It is noteworthy that all the pyrimidine-2,1,3-thiodiazoles synthesized, with the exception of the N-methyl derivatives, were difficult to burn and did not show sharp melting points in contrast to their methyl derivatives, which were used for their identification and whose structures were beyond doubt.

The biological activity of the compounds synthesized was investigated by A. V. Loginov, N. I. Vol'fon, and T. F. Guseva; it was found that all the pyrimidine-2,1,3-thiodiazole derivatives were not toxic and that the greatest activity as regards inhibiting Ehrlich's tumor (in mice) was shown by 4-oxo-6-aminopyrimidine-2,1,3-thiodiazole (IX). We take this opportunity to thank the persons mentioned for the investigations.

EXPERIMENTAL

a) 4,6-Dioxypyrimidine-2,1,3-thiodiazole (VI). A mixture of 12 g of 2,6-dihydroxy-4,5-diaminopyrimidine [4], 120 ml of dry pyridine, 15 ml of thionyl aniline and 4 g of potassium acetate in 25 ml of anhydrous alcohol was boiled for 2 hours in a flask fitted with a stirrer and a reflux condenser, closed with a calcium chloride tube. We observed the evolution of sulfur dioxide and a change in color from yellow to red, which then disappeared. The cooled reaction mixture was freed of potassium sulfate; the latter was washed with hot pyridine, the combined filtrates concentrated to a thick mass, which was cooled and made acid to Congo with 5% hydrochloric acid, and the precipitate washed with water; we obtained 6.5 g of a substance (77%) with m. p. 289-291° (with decomp.); the product was soluble in caustic alkalis and pyridine, sparingly soluble in dioxane and propyl and butyl alcohols and insoluble in ethyl alcohol, benzene, toluene, chloroform, carbon tetrachloride and dichloroethane. It was liberated by acids from an alkaline solution as an amorphous powder.

Found %: N 32.71, 32.91; S 19.19, 18.73. $C_4H_2O_2N_4S$. Calculated %: N 32.95; S 18.32.

b) A mixture of 2 g of 4-oxo-6-aminopyrimidine-2,1,3-thiodiazole (VIII), 50 ml of water and 3.5 ml of sulfuric acid (d 1.84) was heated to 80° and 7 ml of a 40% solution of sodium nitrite gradually added; heating was continued for 30-40 minutes (until solution was complete). After 12 hours, 0.8 g of a yellow precipitate had formed. For identification, the latter was methylated with dimethyl sulfate (5 ml) at 35° for 1 hour; the reaction mixture was extracted with hot chloroform and the residue from evaporation of the chloroform recrystallized from 50° alcohol; the product had m. p. 148-149°. A mixed melting point with authentic 4,6-dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole was not depressed.

4-Oxo-6-thiopyrimidine-2,1,3-thiodiazole (VII). 10 g of 2-thio-6-oxo-4,5-diaminopyrimidine [7], 100 ml of dry pyridine and 15 ml of thionyl aniline was treated as in the previous case to yield 10 g of a substance (84%) with m. p. 286-287° and properties similar to those of (VI).

Found %: N 30.83, 30.46; S 37.27. $C_4H_2ON_4S_2$. Calculated %: N 30.15; S 34.45.

4-Oxo-6-aminopyrimidine-2,1,3-thiodiazole (VIII). 10 g of 6-hydroxy-2,4,5-triaminopyrimidine sulfate, 120 ml of dry pyridine, 15 ml of thionyl aniline and 4 g of potassium acetate in 25 ml of anhydrous alcohol were treated similarly to the previous reaction mixture; we obtained 9 g of a substance (78%), which did not melt even at 400°; it was soluble in alkalis, liberated in the form of an amorphous yellow precipitate on acidification and insoluble in organic solvents.

Found %: N 37.35, 38.16 (for the crude product). $C_4H_3ON_5S$. Calculated %: N 41.40.

4-Oxo-6-aminopyrimidine-2,1,3-thiodiazole hydrochloride. 1 g of (XI) was boiled for 1 hour with 20 ml of 15% hydrochloric acid solution; after purification of the solution with charcoal and concentration of the filtrate in vacuum, the precipitate formed was dried in a vacuum desiccator over sodium hydroxide.

Found %: Cl 17.05, 17.13. $C_4H_3ON_5S \cdot HCl$. Calculated %: Cl 17.31.

4,6-Dioxo-7-methylpyrimidine-2,1,3-thiodiazole (IX). 5 g of 2,6-dioxo-3-methyl-4,5-diaminopyrimidine [8] (IV), 70 ml of glacial acetic acid and 6 ml of thionyl aniline were boiled for 20-25 minutes and the solution obtained was concentrated to the beginning of crystallization. After acidification of the mixture to Congo with 5% hydrochloric acid, the precipitate was collected, washed with water and dried at 100°; we obtained 4.5 g of a substance (77%) with m. p. 212-213° (from 50° alcohol); the product was soluble in alcohol, pyridine and acetic acid and insoluble in benzene, toluene and carbon tetrachloride.

Found %: N 30.56, 30.69. $C_5H_4O_2N_4S$. Calculated %: 30.35.

4,6-Dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole (X). a) 1.5 g of 4,6-dioxypyrimidine-2,1,3-thiodiazole was dissolved in 30 ml of 10% sodium hydroxide solution and 3 ml of dimethyl sulfate was added to the solution obtained over a period of 30 minutes with stirring at 35°. After being stirred for 1 hour at 20°, the solution was extracted with hot chloroform and the chloroform solution evaporated to yield 0.9 g of a substance (52%) with m. p. 148-150°. A mixed melting point with 4,6-dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole (authentic sample) was not depressed.

Found %: N 28.77, 28.57. $C_6H_6O_2N_4S$. Calculated %: N 28.15.

b) 1.5 g of 4,6-dioxo-7-methylpyrimidine-2,1,3-thiodiazole was methylated as in the previous experiment; we obtained 0.6 g of a substance (40%) with m. p. 148-150°. A mixed melting point with authentic 4,6-dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole.

c) 2 g of 4-oxo-6-thiopyrimidine-2,1,3-thiodiazole (VII), 3 g of monochloroacetic acid and 40 ml of water were heated on a water bath for 2 hours and to the cooled solution was added 3 ml of concentrated hydrochloric acid. Heating was continued for a further 1 hour and then the solution was concentrated to crystallization; we obtained 0.75 g of substance. After methylation as in the previous case and recrystallization from 50° alcohol, the substance had m. p. 148-149.5°. A mixed melting point with 4,6-dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole was not depressed.

SUMMARY

1. The reaction of thionyl aniline with aromatic o-diamines was extended to o-diamines of the pyrimidine series, containing 2- and 6-oxo, 2-thio-6-oxo and 2-amino-6-oxo groups; in addition, it was shown that under certain conditions, pyrimidine o-diamines are capable of reacting with thionyl aniline not only as the free bases, but also as their salts.

2. It was shown that under identical conditions the pyrimidinethiodiazole ring is formed much more readily than the benzimidazole ring.

3. It was also shown that 4,6-dioxo- and 4,6-dioxo-7-methylpyrimidine-2,1,3-thiodiazoles are methylated with dimethyl sulfate to give 4,6-dioxo-5,7-dimethylpyrimidine-2,1,3-thiodiazole under the usual conditions for purines.

4. It was shown that 4-oxo-6-aminopyrimidine-2,1,3-thiodiazole undergoes diazotization similarly to guanine to form 4,6-dioxopyrimidine-2,1,3-thiodiazole.

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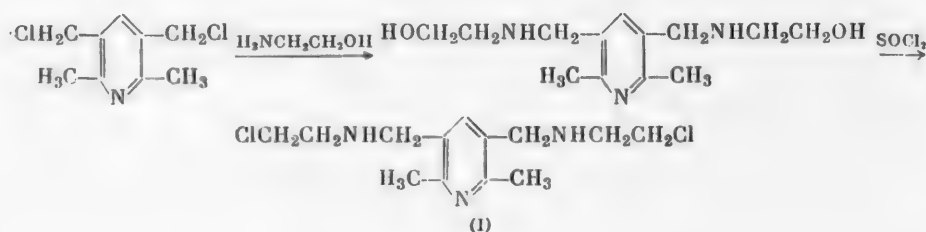
*Original Russian pagination. See C.B. Translation.

SOME HETEROCYCLIC β -CHLOROETHYLAMINES

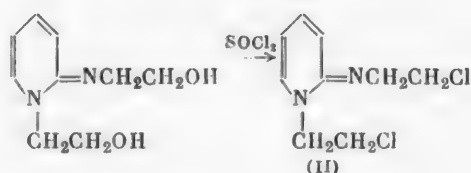
G. I. Braz, V. P. Bronovitskaya, and K. N. Kurdyumova

During a search for anticancer agents, we synthesized two β -chloroethylamino derivatives of the pyridine series, namely, 2,6-dimethyl-3,5-di-(β -chloroethylaminomethyl)-pyridine (I) and N,N'-di-(β -chloroethyl)- α -pyridonimine (II), which differ from the normally used β -chloroethylamines in that their β -chloroethyl groups are on different nitrogen atoms.

For the preparation of 2,6-dimethyl-3,5-di-(β -chloroethylaminomethyl)-pyridine (I), 2,6-dimethyl-3,5-di-(chloromethyl)-pyridine [1] was condensed with monoethanolamine to give 2,6-dimethyl-3,5-di-(β -hydroxyethylaminomethyl)-pyridine, which was purified through the picrate, converted into the hydrochloride, then treated with thionyl chloride and (I) isolated as the trihydrochloride.

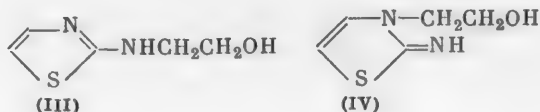


N,N'-Di-(β -chloroethyl)- α -pyridonimine, containing one of its β -chloroethyl groups on the ring nitrogen was synthesized analogously from the previously prepared [2] N,N'-di-(β -hydroxyethyl)- α -pyridonimine.



In addition, we studied the reaction of ethylene oxide with 2-aminothiazole in acetone in the presence of water. The reaction of ethylene oxide with 2-amino-4-methylthiazole was described recently [3]. By distillation, the authors isolated from the reaction mixture a β -hydroxyethyl derivative, to which they ascribed the structure of 3-(β -hydroxyethyl)-4-methyl-2-thiazolonimine in analogy with the reaction product of 2-aminopyridine and ethylene oxide, which was first obtained and investigated by I. L. Knunyants [4]. At first we also attempted to isolate the compounds we obtained by fractionation in vacuum. However, after distillation of the 2-aminothiazole, the weight of which was about half of the amount originally taken, such strong decomposition began that distillation had to be abandoned. Instead, after removal of the unreacted ethylene oxide and acetone, the substances in the reaction mixture were converted into picrates and fractionally crystallized, as a result of which we obtained the picrate of a monohydroxyethyl derivative of 2-aminothiazole in a pure form. This picrate was then converted into the hydrochloride, from which the free base was isolated. In addition, the hydroxyl group was replaced by chlorine by the action of thionyl chloride on the hydrochloride of the β -hydroxyethyl derivative.

To solve the problem of whether the compound we obtained was 2-(β -hydroxyethylamino)-thiazole (III) or, as seemed more probable from the analogy mentioned, 3-(β -hydroxyethyl)-2-thiazolonimine (IV), we subjected it to alkaline hydrolysis. When the hydrochloride of the hydroxyethyl derivative of 2-aminothiazole was boiled with excess 10% sodium hydroxide solution, ammonia was liberated for the first two hours and this seemed to confirm our hypothesis. However, with further heating, besides ammonia, hydrogen sulfide began to form, indicating extensive decomposition. We were unable to isolate from the reaction mixture either the expected 3-(β -hydroxyethyl)-2-thiazolone or any other individual organic compound. Thus, apart from the analogy, there are no data at present to give grounds for choosing between Formulas (III) and (IV). For this reason the structure of the product from the reaction of ethylene oxide with 2-aminothiazole requires further study.



The trihydrochloride of 2,6-dimethyl-3,5-di-(β -chloroethylaminomethyl)-pyridine (I) and N,N'-di-(β -chloroethyl)- α -pyridonimine (II) as its hydrochloride were investigated by Prof. L. F. Larionov and O. V. Zubova. As reported by these authors, the first of the substances ($LD_{100} = 400$ mg/kg) was tested on rats with sarcoma 45, Geren's carcinoma and Ehrlich's tumor, and the second ($LD_{100} = 100$ mg/kg) on rats with sarcoma 45 and Ehrlich's tumor. Neither of the substances showed antitumor activity.

EXPERIMENTAL

2,6-Dimethyl-3,5-di-(β -hydroxyethylaminomethyl)-pyridine. 8 g of 2,6-dimethyl-3,5-di-(chloromethyl)-pyridine was dissolved in 48 g of monoethanolamine; solution was accompanied by heat evolution. The flask was connected to an air condenser, the solution heated for 2 hours on an oil bath at 170-175°, the excess ethanolamine removed in vacuum and the residue dissolved in water and saturated with potassium carbonate. The oil thus liberated was extracted with chloroform, the extract dried with anhydrous sodium sulfate, the chloroform removed and the ethanolamine liberated from the hydrochloride by treatment with potassium carbonate removed by vacuum distillation. The oily residue was repeatedly treated with anhydrous benzene and removal of the benzene from the extract yielded 8.3 g of an oily substance, which crystallized on prolonged standing. In the usual way, 1 g of this oil was converted into the picrate, which was purified by recrystallization from alcohol (350 ml). The yield of the picrate was 2.2 g and the m. p. 192-193°. After a second recrystallization from alcohol, the substance had m. p. 194-195°.

Found %: C 41.98; H 4.27; N 17.80. $C_{13}H_{23}O_2N_3 \cdot 2C_6H_5O_7N_3$. Calculated %: C 42.18; H 4.10; N 17.73.

2.2 g of the picrate with m. p. 192-193° was dissolved in 10 ml of concentrated hydrochloric acid, the liberated picric acid removed by filtration and washed with concentrated hydrochloric acid and the filtrate extracted with benzene. The hydrochloric acid solution was diluted with an equal volume of water and evaporated to dryness in vacuum and the residue treated twice with anhydrous alcohol, which was subsequently distilled, and then treated similarly with anhydrous benzene. The hydrochloride obtained was a solid, hygroscopic substance. The yield was 1.1 g.

2,6-Dimethyl-3,5-di-(β -chloroethylaminomethyl)-pyridine (I). 1.5 g of carefully dried 2,6-dimethyl-3,5-di-(β -hydroxyethylaminomethyl)-pyridine hydrochloride was placed in a flask with a reflux condenser, mixed with 7 ml of thionyl chloride, left at room temperature for 42 hours with protection from atmospheric moisture and shaken periodically by hand and then heated at 40-45° for 2 hours. After the reaction, the excess thionyl chloride was removed in vacuum and the residue treated with anhydrous alcohol, which was subsequently removed by distillation, and recrystallized from alcohol. The 2,6-dimethyl-3,5-di-(β -chloroethylaminomethyl)-pyridine trihydrochloride obtained formed colorless, needle-like crystals. The yield was 1.1 g (55%) and the decomp. p. 220-221°.

Found %: C 39.41; H 6.01; Cl 44.19, 44.46. $C_{13}H_{21}N_3Cl_2 \cdot 3HCl$. Calculated %: C 39.05; H 6.05; Cl 44.38.

N,N'-Di-(β -chloroethyl)- α -pyridonimine (II). With stirring and cooling in ice, a solution of 1.5 ml of thionyl chloride in 2 ml of chloroform was added dropwise to a mixture of 1 g of pure N,N'-di-(β -hydroxyethyl)- α -pyridonimine hydrochloride with 10 ml of chloroform. The crystalline hydrochloride gradually dissolved and

a colorless oil was liberated from the solution. When the thionyl chloride had been added, the mixture was boiled for 3 hours on a water bath until the evolution of gases ceased, the chloroform and excess thionyl chloride removed from the resulting brown solution in vacuum with heating and the oily residue dissolved in anhydrous alcohol and decolorized with charcoal. Evaporation of the filtrate left an oil which could not be crystallized from the usual organic solvents. Mixing an alcohol solution of the oil with an alcohol solution of picric acid precipitated a picrate, which crystallized from alcohol in the form of fine yellow needles with m. p. 150.5-151.5°. The yield was 1.27 g. According to analysis data, this picrate was the monopicate of N,N'-di-(β -chloroethyl)- α -pyridonimine.

Found %: C 40.30; H 3.25; Cl 15.82. $C_9H_{12}N_2Cl_2 \cdot C_6H_3O_7N_3$. Calculated %: C 40.19; H 3.37; Cl 15.79.

By the action of concentrated hydrochloric acid, the picrate was converted into the hydrochloride as indicated above in the preparation of 2,6-dimethyl-3,5-di-(β -hydroxyethylaminomethyl)-pyridine hydrochloride. Evaporation of the hydrochloric acid solution of the hydrochloride in vacuum left a thick colorless oil, which could not be crystallized.

Interaction of ethylene oxide with 2-aminothiazole. a) To a solution of 60 g (0.6 mole) of 2-aminothiazole with m. p. 89-90° in 90 ml of anhydrous acetone was added 12 ml of water, ethylene oxide passed into the solution with cooling in ice and salt until the increase in weight was 27 g (0.61 mole) and the mixture left in a closed vessel at 20-25° for 5 days. The solvent and unreacted ethylene oxide were then removed in vacuum, the residue (66.9 g) dissolved in 30 ml of hot alcohol and 30.8 g of unreacted 2-aminothiazole isolated by freezing the solution with an ice-salt mixture. The alcohol filtrate was heated and mixed with a hot alcohol solution of picric acid and the 2-aminothiazole picrate, which precipitated from the hot solution, rapidly removed to give 20.4 g of yellow needles, melting at 215-216° after recrystallization from alcohol.

Found %: C 32.71; H 2.12. $C_5H_4N_2S \cdot C_6H_3O_7N_3$. Calculated %: C 32.82; H 2.13.

The concentrated alcohol filtrate yielded the picrate of the hydroxyethyl derivative of 2-aminothiazole as yellow platelets. The yield was 16.9 g (19.7% on the 2-aminothiazole reacting) and the m. p. 159-162° (from alcohol). Further recrystallization of the product from alcohol raised the melting point to 161-162°.

Found %: C 35.47; H 3.20; N 18.35. $C_5H_8ON_2S \cdot C_6H_3O_7N_3$. Calculated %: C 35.39; H 2.97; N 18.76.

2 g of the picrate was treated with concentrated hydrochloric acid as given above to yield 1.4 g of the hydrochloride of the β -hydroxyethyl derivative of 2-aminothiazole; after recrystallization from alcohol, the substance had m. p. 137-138°.

Found %: C 33.48; H 5.02; Cl 19.56. $C_5H_9ON_2ClS$. Calculated %: C 33.24; H 4.98; Cl 19.66.

1 g of the hydrochloride was dissolved in 1 ml of water, 2 ml of concentrated sodium hydroxide solution added and the mixture saturated with solid potassium carbonate. This yielded 0.5 g of the β -hydroxyethyl derivative of 2-aminothiazole (III or IV), which melted at 105-106° after 2 recrystallizations from alcohol. The colorless needles were difficultly soluble in ether and benzene.

Found %: C 41.65; H 5.56; N 19.71. $C_5H_8ON_2S$. Calculated %: C 41.66; H 5.55; N 19.44.

To 1 g of the hydrochloride of the β -hydroxyethyl derivative (see above) was added 3 ml of anhydrous chloroform, the mixture cooled to -10° and a solution of 0.5 ml of thionyl chloride in 1 ml of anhydrous chloroform slowly added dropwise with stirring. Stirring with cooling was continued for a further 1 hour and the mixture left at room temperature overnight and then boiled for 2 hours. The brown reaction mixture was evaporated in vacuum, the oily residue treated with a few drops of anhydrous alcohol and stirred with a rod and then the hydrochloride of the β -chloroethyl derivative obtained crystallized spontaneously. The yield of impure substance was 0.75 g (68%) and the m. p. 131-133°. After recrystallization from alcohol (charcoal), the substance had m. p. 132.5-133.5°.

Found %: C 30.36; H 4.13; Cl 35.58. $C_5H_8N_2Cl_2S$. Calculated %: C 30.15; H 4.02; Cl 35.68.

b) The reaction mixture obtained by the interaction of 60 g of 2-aminothiazole with ethylene oxide, as described in Experiment a, was vacuum distilled and 28.45 g of unreacted 2-aminothiazole was collected at 92-125° (3-4 mm). With further distillation, which was accompanied by strong decomposition, the following fractions were collected: 1st with b. p. 152-172° (3 mm), 1.7 g of a thick, oily liquid and 2nd with b. p. 172-

-195° (3 mm), 2.07 g of a thick yellow oil. A considerable amount of tar remained in the distillation flask. Solution of the 2nd fraction in anhydrous alcohol yielded 0.15 g of a substance which crystallized from alcohol as white prisms with m. p. 151-152°, but from which we were unable to obtain a hydrochloride or a picrate.

Found %: C 42.17; H 5.74; N 18.43; S 24.29.

From the alcohol filtrate of this substance and also from an alcohol solution of the 2nd fraction a picrate was precipitated, which crystallized from alcohol as yellow needles. The yield was 0.6 g and the m. p. 163-164°.

Found %: C 35.45; H 2.82; N 17.80.

According to melting point and analysis data, the picrate was similar to that of the hydroxyethyl derivative of 2-aminothiazole. However, a mixture of the two picrates melted at 142-148°. Thus, it was not possible to isolate the β -hydroxyethyl derivative of 2-aminothiazole from any of the fractions. The compounds obtained by fractional distillation were not examined further.

SUMMARY

1. 2,6-Dimethyl-3,5-di-(β -chloroethylaminomethyl)-pyridine and N,N'-di-(β -chloroethyl)- α -pyridonimine were synthesized.

2. The interaction of ethylene oxide with 2-aminothiazole yielded a β -hydroxyethyl derivative, which was either 2-(β -hydroxyethylamine)-thiazole or 3-(β -hydroxyethyl)-2-thiazolonimine, and the corresponding β -chloroethyl derivative was obtained from it.

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SYNTHESIS OF COMPOUNDS OF THE 1-ALKYLTHIOBUTEN-1-YNE-3 TYPE

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Syntheses based on diacetylene are of great theoretical and practical interest. With co-workers, one of us recently considerably extended the study of diacetylene reactions: the mechanism of its formation was elucidated [1], ethers of various alcohols and acetals were synthesized from it [2] and its reactions with thiols were investigated [3]. On the latter problem, the literature contains only a patent claim [4], the authors of which reported that the corresponding monosubstituted butenynes were formed from butanethiol, benzylthiol and mono-thioethylene glycol as the sole reaction products. However, the chemical properties of these compounds were not described.



In a study of the interaction of diacetylene with ethanethiol and thiophenol with excess thiol present in the reaction medium [3], together with 1-ethylthio (and, correspondingly, phenylthio)butenynes, considerable amounts of secondary products, apparently 1,4-diethylthio (and, correspondingly, diphenylthio) butadienes-1,3, were formed.



Secondary products could be expected under these conditions as it was previously established [5] that in the vinylation of thiols, bis-alkylthio-1,2-ethane was formed due to a secondary reaction between vinyl sulfide and the thiol and a considerable excess of acetylene in the reaction medium was necessary to obtain a good yield of vinyl sulfides.



The task of the present investigation was the development of a general method of synthesizing 1-alkylthiobuten-1-yne-3 in maximal yield. For this purpose we largely used the conditions described in [4], changing them by increasing the amount of catalyst, lowering the temperature etc. To a cooled solution of diacetylene (1.2-1.3 moles per mole of thiol) in slightly alkaline methanol (4-5 mol. % of KOH, calculated on the thiol) was added the appropriate alkyl thiol in a stream of dry nitrogen, after which the reaction mixture was heated slightly. Under these conditions it was possible to isolate alkylthiobutenynes as the sole reaction product in a yield of 72-80%, calculated on the thiol. The corresponding methyl derivative was an exception, though it was obtained as the sole reaction product but only in 50% yield, which was connected with losses of gaseous methane thiol during the synthesis. The addition of hydroquinone to the reaction mixture did not reduce the yield, indicating the ionic nature of the reaction of diacetylene with thiols.

The reaction of diacetylene with thiol ions apparently proceeds much more readily than with alkoxyls, i.e., the same rule is observed as in the reaction of acetylene with alcohols and thiols [6, 7]; therefore it is possible to vinylate or vinyl ethynylate thiols readily in alcohols without touching the hydroxyl groups of the latter.

TABLE 1

RSCH = CH - C \equiv CH

R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Yield (% on thiol)
				found	calc.	
CH ₃	54°(15)	1.5578	0.9763	32.40	30.70	50
C ₂ H ₅ *	63—64 (14)	1.5449	0.9581	36.81	35.35	70—72
C ₃ H ₇	66—68 (6)	1.5340	0.9383	41.81	39.96	78—79
C ₄ H ₉ **	73—75 (3)	1.5240	0.9130	46.09	44.56	72—80

* According to literature data: b. p. 65-65.5° (17 mm), n_D^{20} 1.5468, d_4^{20} 0.9516 [3].

** According to literature data: b. p. 80-82° (8 mm) [4].

The thiobutenynes obtained (Table 1) were substances which readily became yellow in air, but could be stored unchanged in the cold in ampoules which had first been flushed with nitrogen. It was not possible to obtain them in a completely colorless form.

TABLE 2 *

Substance	C=C		C \equiv C		Source **
	ν cm ⁻¹	intensity χ cm ⁻¹	ν cm ⁻¹	intensity χ cm ⁻¹	
HC \equiv C-CH=CHSC ₄ H ₉	2110	310	1560	620	Our data
HC \equiv C-CH=CH ₂	2096	—	1600	—	[8a]
HC \equiv CR	2150—2200	—	—	—	[8a,b,c]
RCH=CHR-cis	—	—	1650	25—250	[8b,c,d]
RCH=CHR-trans	—	—	1670	10—100	[8c,d]

* Literature data on the intensities of the absorption bands were reduced to the same intensity dimensions.

** The infrared spectrum was plotted by B. V. Lopatin, to whom the authors are grateful.

The characteristic frequencies in the infrared absorption spectra of the compounds obtained were determined (Table 2). A comparison with the spectra of corresponding hydrocarbons of the ethylene and acetylene series [8] shows that the spectra of alkylthiobutenynes are distinguished by a high intensity and a reduced frequency both for the C \equiv C and to a lesser extent for the C=C groupings.

TABLE 3

CH \equiv C-CH=CHSR R=	Equivalent	
	found	calc.
CH ₃	97.87; 97.29	98.17
C ₂ H ₅	112.08; 111.96	112.19
C ₃ H ₇	125.72; 125.98	126.22
C ₄ H ₉	139.41; 139.27	140.25

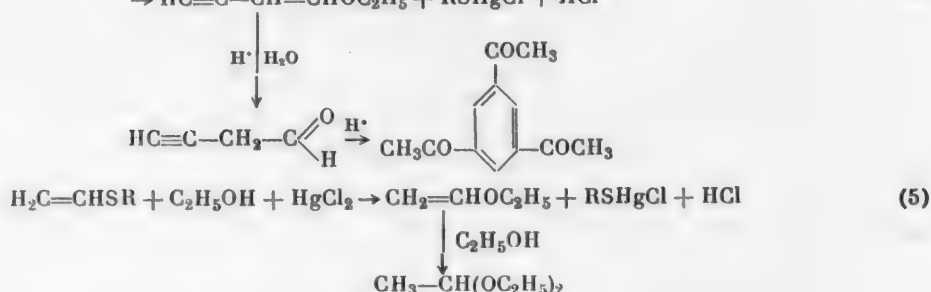
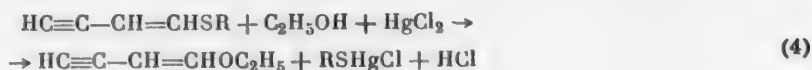
* See also [3].

This indicates the presence of appreciable conjugation in the molecule as was also confirmed by noticeable molecular refraction increments (1.5-1.8).

When treated with mercuric chloride in 96% alcohol, all the alkylthiobutenynes liberated an equimolecular amount of HCl and the mercury chloride of the corresponding thiol, i. e., underwent cleavage analogous to that which we demonstrated previously for alkylthioethylene compounds [5]. * Table 3 gives the equivalents, calculated from titration of the acid liberated.

It is interesting that when this reaction was carried out in anhydrous alcohol, rapid tar formation began even with cooling.

In an aqueous alcohol medium it was possible to isolate triacetylbenzene and, apparently, butyn-3-ol-1 together with the alkylmercury chloride and HCl. This indicates the particular tendency toward hydrolysis of ethoxybutenyne, which must be formed in this case as the primary reaction product (see Equation 4) in analogy with the reaction of alkylthioethylenes, illustrated by Equation 5 [5]. The expected ethyl acetals of acetoacetic ester could not be isolated from the reaction medium.



EXPERIMENTAL

Synthesis of 1-alkylthiobuten-1-yne-3. For the synthesis we used industrial ethanethiol and propanethiol; butanethiol was obtained from butyl bromide and thiourea [9], methanethiol from S-methylthiourea sulfate [10] and diacetylene from 1,4-dichlorobutyne-2 [2, 12].

1-Butylthiobuten-1-yne-3. Into a three-necked flask fitted with a reflux condenser, stirrer, dropping funnel and thermometer, we placed 100 g of anhydrous methyl alcohol and 0.25 g of powdered potassium hydroxide. Then, with a moderate stream of nitrogen, which was continued until the end of the synthesis, and cooling to -10° , into the reaction flask was introduced first 7 g of diacetylene and then 9 g of butanethiol. Stirring at -10° was continued for half an hour and then the reaction product was heated at $50-52^\circ$ for a further 3 hours. The mixture was left overnight. The bulk of the methyl alcohol was evaporated in vacuum (to a volume of 25-30 ml). The residue was dissolved in 150 ml of ether, washed 5 times with distilled water and dried over sodium sulfate. After removal of the ether, the dark brown liquid was distilled to give 11 g (80%) of substance.

Found %: C 68.03; H 8.81; S 22.69. $\text{C}_8\text{H}_{12}\text{S}$. Calculated %: C 68.44; H 8.62; S 22.94.

1-Propylthiobuten-1-yne-3. From 7.6 g of propanethiol and 7 g of diacetylene we obtained 10 g (74%) of product.

Found %: C 66.52; H 7.97; S 24.91. $\text{C}_7\text{H}_{10}\text{S}$. Calculated %: C 66.61; H 7.98; S 25.41.

1-Ethylthiobuten-1-yne-3. From 12.4 g of ethanethiol and 15 g of diacetylene we obtained 16 g (71%) of product.

Found %: C 64.09; H 7.32; S 28.39. $\text{C}_6\text{H}_8\text{S}$. Calculated %: C 64.23; H 7.19; S 28.58.

1-Methylthiobuten-1-yne-3. S-Methylthiourea sulfate was decomposed with aqueous alkali as described in [10]; the methanethiol liberated was collected in a cooled trap and then evaporated into the reaction medium in a stream of nitrogen. From 8 g of methanethiol and 16 g of diacetylene we obtained 8.1 g (50%) of substance.

Found %: C 61.21; H 6.32; S 32.31. $\text{C}_5\text{H}_6\text{S}$. Calculated %: C 61.16; H 6.18; S 32.66.

Reaction of alkylthiobutenynes with mercuric chloride. a) For quantitative titration of small samples, 0.001-0.0015 mole of alkylthiobutenyne and 3-5 ml of a 20% solution of HgCl_2 in 96% ethanol (approximately two moles per mole of alkylthiobutenyne) were placed in a conical flask. Precipitation of the alkylthiomercury chloride began immediately. After 24 hours, 5 ml of water was added and the acid titrated with 0.1 N NaOH (in the presence of methyl orange or potentiometrically). The results are presented in Table 3.

b) 7 g (0.05 mole) of butylthiobutenyne was diluted with an equal volume of 96% alcohol and added dropwise with stirring to a solution of 13.6 g (0.05 mole) of mercuric chloride in 70 ml of the same alcohol, cooled

with ice water, at such a rate that the temperature of the reaction medium did not exceed 4-5°. Stirring was then continued at 4-5° for 2 hours and the mixture left at normal temperature for a further 48 hours; the precipitate of butylthiomercury chloride collected and washed with alcohol [weight 15.5 g (96%)]. After recrystallization from dioxane, the substance had m. p. 176-177° (literature data [11] for C_4H_9SHgCl : m. p. 177-177.5°). Titration of part of the alcohol solution with 0.1 N NaOH indicated 0.48 mole (96%) of HCl. The bulk of the HCl was neutralized with anhydrous sodium carbonate and the alcohol evaporated at 25-30 mm and collected in a trap (negative reaction for an acetylene bond). Distillation of the residue yielded 1.9 g (60%) of a substance which readily formed a tar when distilled, gave a reaction for an aldehyde and had b. p. 27-28° at 27 mm and n_D^{20} 1.4475 (for butyn-3-al-1, b. p. 40° at 100 mm and n_D^{20} 1.4455 [12]). During storage, the precipitation of triacetylbenzene crystals (m. p. 160-162°, mixed m. p. with authentic triacetylbenzene 161-163°) soon began.

SUMMARY

1. A method is given for the synthesis of 1-alkylthiobuten-1-yne-3 in 70 to 80% yields, which consists of the reaction of thiols with excess diacetylene in methanol in the presence of potassium hydroxide.
2. The presence of strong conjugation in alkylthiobutenyne molecules was demonstrated by infrared spectroscopy.
3. It was shown that the interaction of alkylthiobutenynes with mercuric chloride in aqueous alcohol resulted in the quantitative formation of hydrogen chloride, alkylthiomercury chloride and hydrolysis products of the butenyne part of the molecule.

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MECHANISM OF THE REACTION BETWEEN THIOLS
AND 1-ALKYLTHIOBUTENYNES AND SOME PROPERTIES
OF BIS-ALKYLTHIOBUTADIENES

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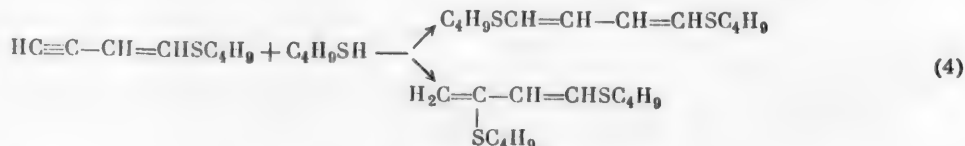
Together with co-workers, one of us [1] showed that besides producing substituted butenynes, the reaction of diacetylene with excess thiol forms secondary products which apparently have the structure of 1,4-bis-substituted butadienes-1,3.



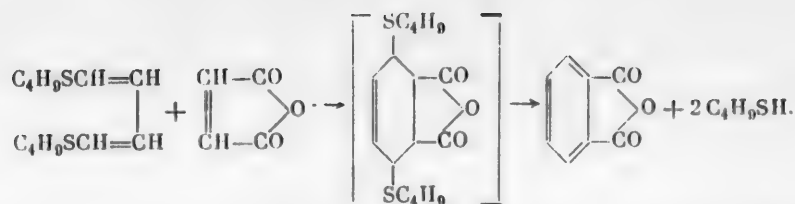
The reaction of diacetylene with thiols (Equation 1) has an ionic character as it is accelerated by alkalis, but not by azoisobutyronitrile [1] and is not retarded by the presence of hydroquinone [2]. It seemed interesting to elucidate the nature of the reaction between alkylthiobutenynes and thiols (Equation 2). For this purpose we thoroughly investigated the reaction between butanethiol and 1-buthylthiobutenyne-3. Our experiments showed that this reaction has all the main characteristics of free radical processes: it was accelerated in the presence of atmospheric oxygen and azoisobutyronitrile and by heating, while replacement of air by nitrogen and the addition of thiols to monosubstituted ethylenes results in the quantitative formation of addition products contrary to Markovnikov's rule. Vinyl sulfides react with thiols quite vigorously (with the evolution of heat) [3].



Butanethiol reacted with butylthiobutenyne much less vigorously and heating was required for rapid completion of the reaction. The thiol apparently added at the terminal acetylene bond. Neither the chemical nor the optical data we had available made it possible to establish conclusively whether this gave only a 1,4-bis-substituted diene or a mixture of 1,4- and 1,3-bis-substituted dienes with very similar boiling points.



In any case, the 1,4-isomer content was not less than 70% as the bis-buthylthiobutadiene obtained (like the bis-ethylthio- and phenylthiobutadienes prepared previously [1]) condensed with maleic anhydride under drastic conditions to give up to 70% of phthalic anhydride and butanethiol due to cleavage of the adduct formed as an intermediate.



The infrared absorption spectrum of the bis-butylthiobutadiene obtained (see figure) had two bands in the region of the C=C bond, 1580 and 1540 cm^{-1} . There are two possible explanations for this. 1) The product is a 1,4-substituted diene-1,3, but in the form of a mixture of geometric isomers present as rotation forms with *cis*- and *trans*-configurations. The existence of such isomeric forms has been established for other butadiene derivatives [4]. 2) The product is a mixture of 1,4- and 1,3-substituted butadienes-1,3 of which the latter has two somewhat

different absorption bands in the C=C bond region. The ease with which the bis-butylthiobutadiene obtained was oxidized in air, causing the product to become quite yellow, serves as some confirmation that unsymmetrical 1,3-substituted diene was present. The absorption spectrum of even freshly distilled product had a weak band in the region characteristic of carbonyl frequencies (1680 cm^{-1}) (Curve 2). The intensity of this band increased strongly when the product was oxidized for a long time in air (Curve 1). The mechanism and products of this reaction should be studied further.

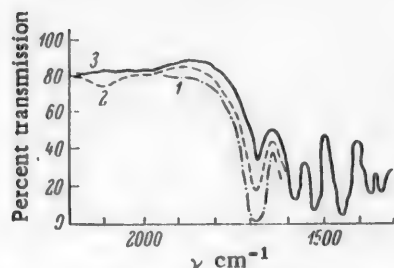


Fig. 1. Infrared absorption spectrum of the product obtained by reaction of 1-butylthiobuten-1-yne-3 with butanethiol. 1) Sample oxidized by air; 2) sample after one distillation; 3) sample after many distillations.

The infrared spectrum of bis-butylthiobutadiene, plotted in the presence of atmospheric oxygen, had a weak band in the region of 2100 cm^{-1} , i. e., corresponding to an acetylene band. After numerous redistillations, a product was obtained which had no absorption in this region (Curve 3). It is possible that this band was due to traces (not more than 5%) of butynal thioacetal $\text{CH}_3\text{C}\equiv\text{CCH}(\text{SC}_4\text{H}_9)_2$ of the isomeric 1,2-bis-butylthiobutyne-3 $\text{HC}\equiv\text{CCH}(\text{SC}_4\text{H}_9)\text{CH}_2\text{SC}_4\text{H}_9$. We could not isolate these impurities in an individual form.

We attempted unsuccessfully to direct the addition of thiols to butylthiobutenynes by an ionic route, using various acid and alkaline catalysts and hoping to change the ratio of isomers in the reaction mixture. All these experiments were carried out in a nitrogen atmosphere or in ampoules from which air had been removed. However, even under these conditions residual traces of oxygen were sufficient to produce free radical addition. Potassium butyl mercaptide did not have any effect on the course of the reaction. Triethylamine and sulfur dioxide are antioxidants and in this capacity they lowered the yield of addition product, but they did not produce ionic catalysis. The infrared absorption curves of bis-butylthiobutadienes, obtained in the presence of the above substances, coincided with each other completely, indicating the identity of the compounds. It is possible, however, that ionic addition of thiols could be achieved with more active catalysts.

We also studied the reaction between butanethiol and methylthio- and ethylthiobutenynes in order to prepare bis-alkylthiobutadienes with different radicals.



We discovered that such substituted butadienes were partially symmetrized to form mixtures of butadienes with the same type of radical.



Due to the similarity of the boiling points of the components of the mixture, not all the expected products could be obtained in an analytically pure form.* However, the data in Table 1 show the similarities in the

* As the products were unstable, they had to be distilled at 10^{-2} to 10^{-3} mm so that it was quite impossible to use fractionating columns.

constants of the bis-butylthiobutadienes obtained by addition or symmetrization of the corresponding compounds with different radicals.

The characteristic absorption frequencies of the fractions obtained in the synthesis of bis-butylthiobutadiene and symmetrization of ethylbutylthiobutadiene are compared in Table 2. These data confirm that all the fractions had the same butadiene structure. Thus, symmetrization undoubtedly occurred. The conditions and mechanism of this interesting reaction will be the subject of further investigation.

TABLE 1

Products from the Reaction of Butanethiol and Alkylthiobutenynes $RSCH=CH-C\equiv CH$

R	Fraction number	Proposed structure	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	M_R	
						found	calculated
C_4H_9	1	$C_4H_9SCH=CH-CH=CHSC_4H_9$	83–85° (0.03)	1.5678	0.9745	77.27	72.53
C_4H_9	1	$C_2H_5SCH=CH-CH=CHSC_2H_5$	56–57 (0.03)	1.5898	0.9959	59.17	54.15
	2	$C_2H_5SCH=CH-CH=CHSC_4H_9$	70–72 (0.03)	1.5850	0.9900	68.51	63.46
	3	$C_4H_9SCH=CH-CH=CHSC_4H_9$	83–85 (0.03)	1.5675	0.9745	77.27	72.53
CH_3	1	$CH_3SCH=CH-CH=CHSCH_3$	97–98 (2)	1.6124	1.0210	49.82	44.91
	2	$CH_3SCH=CH-CH=CHSC_4H_9$	64–66 (0.03)	1.5900	1.0030	63.37	58.85
	3	$C_4H_9SCH=CH-CH=CHSC_4H_9$	81–83 (0.03)	1.5680	0.9740	77.57	72.53

TABLE 2

Infrared Absorption Spectra of Bis-Alkylthiobutadienes

Symmetrization products of 1-ethylthio-4-butylthiobutadienes*			Bis-butylthiobutadiene ν cm^{-1}
1st fraction ν cm^{-1}	2nd fraction ν cm^{-1}	3rd fraction ν cm^{-1}	
1678	1674	1674	1678
1588	1588	1582	1586
1538	1538	1530	1532
1448	1448	1450	1450
1378	1378	1376	1376
1348	1348	1348	1344

* See Table 1.

** From butanethiol and butylthiobutenyne.

EXPERIMENTAL

For the synthesis we used butanethiol obtained from butyl bromide and thiourea [5] and 1-alkylthiobuten-1-yne-3 of various compositions which were obtained from thiols and diacetylene by the method we described previously [2]. All the bis-alkylthiobutadienes were examined by infrared spectroscopy. The spectra were plotted over the range $2500-1250$ cm^{-1} on an IKS-11 single-beam infrared spectrometer with a rock salt (NaCl) prism. The spectrum was traced with a pen on the chart of a recording instrument (electronic potentiometer ÉPP-09). The slit width over the whole measurement region was approximately 20 cm^{-1} (19.6 cm^{-1} for the region of 2000 cm^{-1} and 18.1 cm^{-1} at 1500 cm^{-1}). The spectra of all the substances were plotted using the same sylvite

* For a series of samples the spectra were plotted over the range $2500-1000$ cm^{-1} .

TABLE 3
Interaction of Butanethiol and 1-Butythiobuten-1-yne-3 under Various Conditions

Expt. No.	Reagents used			Reaction conditions			Reaction products		
	1-butythiobuten-1-yne-3 (in moles) (A)	thiols (in moles)	catalysts		heating	duration (in hours)	procedure	boiling point (pressure in mm)	yield (in % on A)
			name	(in mol. % on A)					
1	0.07	0.11	-	-	70-80°	9	a	80-82° (0.03)	77
2	0.07	0.11	-	-	70-80°	12	b	85-87° (0.03)	70
3	0.08	0.77	Azoisobutyro-dinitrile	1.1	70-80°	12	b	81-82° (0.03)	75
4	0.05	0.77	-	1.8	50-60°	6	b	85-87° (0.03)	50
5	0.05	0.05	Triethylamine	2.0	50-60°	6	b	83-85° (0.03)	17
6*	0.025	0.033	-	-	50-60°	6	b	81-82° (0.03)	25
7	0.025	0.05	SO ₂	-	50-60°	6	c	-	-
8	0.05	0.054	C ₄ H ₉ SK	1.8	70-80°	12	b	81-82° (0.03)	68

Note: a) Experiment in a flask in a stream of nitrogen; b) experiments in ampoules with preliminary flushing with nitrogen; c) a gentle stream of sulfur dioxide was passed into the ampoule with the substance for 6 minutes, the air was pumped out (to 5 to 7 mm) after the mixture had been frozen and then the ampoule was sealed.

* Hydroquinone (3.6 mol. % to A) was used as an antioxidant in this experiment.

cell with a liquid layer thickness of 0.05 ± 0.001 mm. The accuracy with which the position of the absorption bands in the spectrum (frequencies) was measured was $\pm 10 \text{ cm}^{-1}$ for the region of 2500 cm^{-1} and approximately $\pm 5 \text{ cm}^{-1}$ at 1250 cm^{-1} . The accuracy of measurement of the transmissions of the samples was about $\pm 10\%$ at values of from 10 to 75%.

Synthesis of bis-butythiobutadiene. Into a three-necked flask, fitted with a reflux condenser, mechanical stirrer, dropping funnel and thermometer, was placed 10 g of 1-butythiobuten-1-yne-3 (b. p. $73-75^\circ$ at 3 mm and n_D^{20} 1.5240), and 10 g of butanethiol was gradually added with stirring (in a nitrogen atmosphere); no heat evolution was observed. The mixture was heated at $70-75^\circ$ for 9 hours. Distillation yielded the following fractions: 1st b. p. $124-126^\circ$ (1.5 mm), n_D^{20} 1.5512, 0.5 g; 2nd b. p. $147-149^\circ$ (1.5 mm), n_D^{20} 1.5678, 12.5 g (77%). There was 1.5 g of tarry residue. Individual substances could not be isolated from the 1st fraction after redistillation. Redistillation of the 2nd fraction yielded a substance with b. p. $85-87^\circ$ (0.03 mm), n_D^{20} 1.5680, d_4^{20} 0.9745. The infrared absorption spectrum of this substance after one distillation (Curve 2), many distillations (Curve 3) and oxidation in air for 24 hours (Curve 1) are presented in the figure.

Found %: C 62.58; H 9.58; S 27.57. $C_{12}H_{22}S_2$. Calculated %: C 62.54; H 9.63; S 27.83

This reaction was studied in detail under different conditions and the results are presented in Table 3.

Condensation of bis-butythiobutadiene with maleic anhydride. In an ampoule, previously flushed with nitrogen, were mixed 9 g of bis-butythiobutadiene (from Experiment 2), 3.8 g of maleic anhydride and 25 ml of cryoscopic benzene; the sealed ampoule was heated for 10 hours at 130° . After removal of the benzene and butanethiol, the residue was recrystallized from ligroine to give 3.82 g (66%) of phthalic anhydride, which melted at 130.6° and did not depress the melting point of a pure sample. Treatment of the liquid distillate with mercuric chloride in alcohol and subsequent titration of the liberated hydrochloric acid with alkali indicated the presence of 5.15 g (75%) of butanethiol. A similar condensation of maleic anhydride with the substance obtained from Experiment 8 (in the presence of potassium butyl mercaptide) yielded phthalic anhydride with m. p. 130.9° (67%). Treatment of the distillate showed the presence of butanethiol (74%).

Synthesis of ethylthiobutylthiobutadiene-1,3. In an ampoule previously flushed with nitrogen were mixed 15 g (0.134 mole) of 1-ethylthiobuten-1-yne-3 (b. p. $63-64^\circ$ at 14 mm and n_D^{20} 1.5449), 14 g (0.155 mole) of butanethiol and 0.15 g of azoisobutyronitrile and the ampoule sealed and heated at $70-80^\circ$ for 16 hours. The residue after distillation of the unreacted reagents was repeatedly distilled in high vacuum to give three fractions: the 1st (4 g, 34%) was close in properties to bis-ethylthiobutadiene.

B. p. $56-57^\circ$ (0.03 mm), n_D^{20} 1.5898.

Found %: C 57.77; H 8.61; S 32.95. $C_8H_{14}S_2$. Calculated %: C 55.12; H 8.09; S 36.79.

The second (12 g, 44%) was ethylthiobutylthiobutadiene.

B. p. $70-72^\circ$ (0.03 mm), n_D^{20} 1.5850.

Found %: C 58.71; H 8.87; S 31.44. $C_{10}H_{18}S_2$. Calculated %: C 59.41; H 8.91; S 31.69.

The third (3 g, 20%) was bis-butythiobutadiene.

B. p. $83-85^\circ$ (0.03 mm), n_D^{20} 1.5675.

Found %: C 61.84; H 9.67; S 28.35. $C_{12}H_{22}S_2$. Calculated %: C 62.55; H 9.63; S 27.83.

Table 2 gives the characteristic absorption frequencies of all three fractions.

Synthesis of methylthiobutylthiobutadiene-1,3. The reaction was in an ampoule as in the previous synthesis. From 7 g of butanethiol (0.077 mole) and 7 g (0.071 mole) of 1-methylthiobuten-1-yne-3 (b.p. 54° at 14 mm and n_D^{20} 1.5578) we obtained 10 g of substance. Three fractions were isolated after repeated distillation.

According to analysis, fraction 1 (2 g, 22%) was similar to bis-methylthiobutadiene.

B. p. $97-98^\circ$ (2 mm), n_D^{20} 1.6124.

Found %: C 51.38; H 7.36; S 38.12. $C_6H_{10}S_2$. Calculated %: C 51.46; H 7.24; S 41.30.

According to analysis, fraction 2 (4.5 g, 33%) was similar to methylthiobutylthiobutadiene.

B. p. $64-66^\circ$ (0.02 mm), n_D^{20} 1.5900.

Found %: C 57.07; H 8.60; S 32.35. $C_9H_{16}S_2$. Calculated %: C 57.39; H 8.56; S 34.05

Fraction 3 (1 g, 12%) was bis-butylthiobutadiene.

B. p. 83-84° (0.03 mm), n_D^{20} 1.5630.

Found %: C 61.65; H 9.48; S 28.30. $C_{12}H_{22}S_2$. Calculated %: C 62.55; H 9.63; S 27.83.

SUMMARY

1. Using the reaction between butanethiol and 1-butythiobuten-1-yne-3 as an example, we proved the free radical nature of the interaction between alkyl thiols and alkylthiobutenynes.
2. It was shown optically that the reaction products have the structure of bis-alkylthiobutadienes-1,3, substituted mainly in the 1,4-position.
3. Symmetrization of bis-alkylthiobutadienes with different types of radicals was proved for the first time.

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CYCLOPROPANES AND CYCLOBUTANES

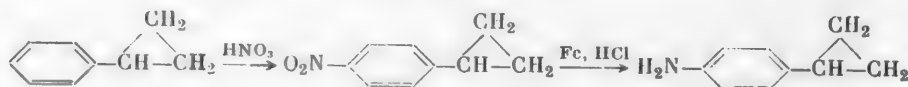
VI. • p-NITROPHENYL- AND p-AMINOPHENYLCYCLOPROPANES

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In previous reports we described some chemical properties of arylcyclopropanes and the opening of the three-membered ring in them under the action of mercury acetate in an aqueous or an alcohol solution [1, 2] and by interaction with aromatic hydrocarbons (and their derivatives) in the presence of aluminum chloride [3]. Arylcyclopropanes behave similarly to styrenes in these addition reactions. An investigation of the Raman and ultraviolet absorption spectra showed [4, 7] that the three-membered ring in arylcyclopropanes is capable of conjugation with an aromatic nucleus, similarly to the double bond in styrenes.

In the present work, we investigated the behavior of phenylcyclopropane in a typical substitution reaction, namely, nitration. We developed a procedure for nitrating phenylcyclopropane, which made it possible to obtain the mononitro derivative in high yields (70-75%). Phenylcyclopropane was nitrated by treatment with fuming nitric acid in acetic anhydride at -50° . •• The position of the nitro group in the nitro compound obtained was determined by oxidation. It was shown that this nitro compound was hardly oxidized by neutral and alkaline solutions of potassium permanganate; it could be oxidized under the conditions used for the oxidation of nitrotoluenes [6], i. e., heating with potassium bichromate in 50% sulfuric acid. The oxidation product was p-nitrobenzoic acid (75% yield); consequently, the nitro group entered the para-position of the benzene ring. The p-nitrophenylcyclopropane obtained was then reduced to the corresponding amine.



The ultraviolet absorption spectrum of p-aminophenylcyclopropane was found to be quite similar to those of arylcyclopropanes [4] and differed from the spectrum of the starting nitro compound, which did not have sharply expressed characteristic maxima and minima* •• (see figure). ••••

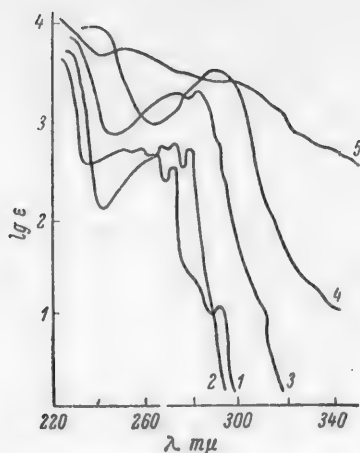
The nitration product of phenylcyclopropane was finally shown to have the structure of nitrophenylcyclopropane by conversion of the amino compound prepared from it into the original phenylcyclopropane. The amino group was removed by treating the diazotized amine with an alkaline solution of formaldehyde.

* For Reports I-V see: Bull. Moscow State University, Chemistry, No. 1, 170 (1957); No. 5, 145 (1957); Bull. Acad. Sci. USSR, Div. Chem. Sci. 121, 303 (1958); Bull. Moscow State University, Chemistry, No. 5, 201 (1958); J. Gen. Chem. 29, 44 (1959). See C. B. translation of Bull. Acad. Sci. USSR and J. Gen. Chem.

•• An example of direct nitration of arylcyclopropanes is described in the literature. Thus, 1,1-diphenylcyclopropane was treated with a mixture of fuming nitric acid, acetic acid and acetic anhydride at -5° to give 1,1-di-p-nitrophenylcyclopropane [5].

••• The absence of characteristic traits in the ultraviolet absorption spectra is typical of most nitro compounds.

•••• All the spectra were plotted on an SF-4 spectrometer; isooctane was used as a solvent.



Ultraviolet absorption spectra. 1) Phenylcyclopropane: λ_{\min} 238, $\lg \epsilon_{\min}$ 2.56; λ_{\max} 267, $\lg \epsilon_{\max}$ 2.66; λ_{\min} 271, $\lg \epsilon_{\min}$ 2.30; λ_{\max} 274, $\lg \epsilon_{\max}$ 2.56; 2) p-tolylcyclopropane: λ_{\min} 244, $\lg \epsilon_{\min}$ 2.06; λ_{\max} 271, $\lg \epsilon_{\max}$ 2.74; λ_{\min} 272, $\lg \epsilon_{\min}$ 2.71; λ_{\max} 274, $\lg \epsilon_{\max}$ 2.75; 3) p-anisylcyclopropane: λ_{\min} 248, $\lg \epsilon_{\min}$ 2.98; λ_{\max} 279, $\lg \epsilon_{\max}$ 3.26; λ_{\min} 282, $\lg \epsilon_{\min}$ 3.21; λ_{\max} 285, $\lg \epsilon_{\max}$ 3.25; 4) p-aminophenylcyclopropane: λ_{\max} 238, $\lg \epsilon_{\max}$ 3.99; λ_{\min} 263, $\lg \epsilon_{\min}$ 2.99; λ_{\max} 288, $\lg \epsilon_{\max}$ 3.48; 5) p-nitrophenylcyclopropane: λ_{\min} 240, $\lg \epsilon_{\min}$ 3.68; λ_{\max} 252, $\lg \epsilon_{\max}$ 3.75.

we investigated the behavior of p-nitrophenylcyclopropane with mercury acetate in a reaction that is characteristic of alkyl- and arylcyclopropanes. It was found that the three-membered ring in p-nitrophenylcyclopropane was not opened by mercury acetate under conditions under which phenylcyclopropane [1] and p-tolyl- and p-anisylcyclopropanes [2] are completely converted into the corresponding γ -mercurated alcohols. The stability of p-nitrophenylcyclopropane to oxidation and its behavior in the reaction with mercury acetate show that the introduction of such a substituent as a nitro group into the benzene nucleus considerably increases the stability of the three-membered ring attached to it.

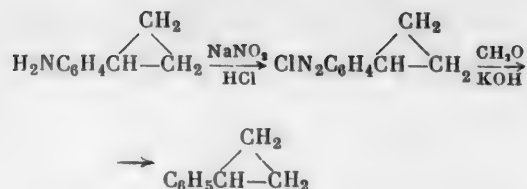
EXPERIMENTAL

Nitration of phenylcyclopropane. Fuming nitric acid (40 ml, d 1.5) was added dropwise with continuous and vigorous stirring to acetic anhydride (150 ml), cooled to -50° . After the remaining nitric acid had been washed from the dropping funnel with acetic anhydride, phenylcyclopropane (35 g) was added (the temperature of the reaction mixture was not allowed to rise above -40°). Stirring was continued for a further half hour at -40 to -35° and then the cold reaction mixture was poured in small portions into 400 ml of boiling water. The oily layer liberated was separated and then combined with an ether extract (150 ml of ether) of the aqueous layer. The ether solution of the nitro compound obtained was washed with water, 2 N sodium carbonate solution and again with water and dried with calcium chloride. The residue after removal of the ether was vacuum distilled. The p-nitrophenylcyclopropane (34 g, 72%) had the following constants:

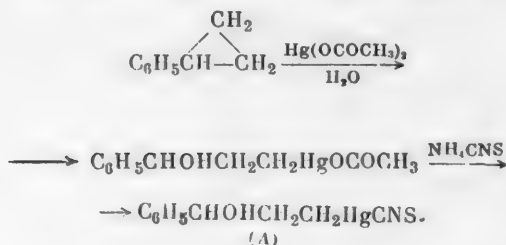
B. p. 106° (5 mm), n_D^{20} 1.5613, d_4^{20} 1.1672, M_R 45.29. $C_9H_9O_2N$. Calculated 44.86.

Found %: C 66.16, 66.32; H 5.80, 5.68; N 8.63. $C_9H_9O_2N$. Calculated %: C 66.24; H 5.52; N 8.53.

* The temperature of the reaction mixture was not raised above -25° as the reaction could then have proceeded explosively.



The hydrocarbon obtained was identified as phenylcyclopropane by its constants and by preparing from it a crystalline organomercury compound (A), which had been described previously by one of us (a mixed melting point with a sample from authentic phenylcyclopropane was not depressed).



It was thus established that under our conditions, the phenylcyclopropane is nitrated in the para-position of the benzene nucleus and that the three-membered ring is not touched.

In order to study the effect of the nitro group in the benzene nucleus of phenylcyclopropane on the reactivity of the three-membered ring

Oxidation of p-nitrophenylcyclopropane. With stirring, 38 ml of concentrated sulfuric acid was added dropwise to a mixture of 3.5 g of p-nitrophenylcyclopropane and a solution of 30 g of sodium bichromate in 60 ml of water; the reaction mixture was boiled for 1 hour and poured into cold water. The precipitated crystals were washed with 2 N sulfuric acid and dissolved in alkali and the p-nitrobenzoic acid reprecipitated by the addition of sulfuric acid. The p-nitrobenzoic acid obtained (2.7 g, 76%) melted at 237-238° (from alcohol). Literature data [6]: m. p. 237-238°. A mixed melting point of the acid obtained with an authentic sample of p-nitrobenzoic acid was not depressed.

Treatment of p-nitrophenylcyclopropane with mercury acetate was under the conditions under which the three-membered ring of phenyl- [1], p-tolyl- and p-anisylcyclopropanes [2] were readily opened: 3 g of p-nitrophenylcyclopropane was shaken for a day with a solution of 6 g of mercury acetate in 22 ml of water. The p-nitrophenylcyclopropane which did not react with mercury acetate was separated and the aqueous solution extracted with ether; normal treatment of the ether solution and evaporation of the ether yielded 2.8 g of unchanged p-nitrophenylcyclopropane with b. p. 110° (7 mm), n_D^{20} 1.5630 and d_4^{20} 1.1700.

Reduction of p-nitrophenylcyclopropane. A mixture of 6.3 g of p-nitrophenylcyclopropane, 6 g of fine iron filings, 6 ml of concentrated hydrochloric acid, 6 g of calcium chloride and 25 ml of water was boiled carefully for 1 hour with stirring; then 3 g of iron filings and 10 ml of concentrated hydrochloric acid were added and heating continued for a further 40 minutes. Alkali was added to the reaction mixture (to a strongly alkaline reaction) and the amine formed was steam distilled. The distillate was extracted with ether; the ether extract dried with potassium hydroxide, the ether removed and the residue vacuum distilled. The yield of p-aminophenylcyclopropane was 3.5 g (65%).

B. p. 105° (9 mm), n_D^{20} 1.5811, d_4^{20} 1.0291, M_R^D 43.11. $C_9H_{11}NF_3\Delta$. Calculated 42.97.

Found %: N 10.62, 10.56. $C_9H_{11}N$. Calculated %: N 10.45.

The benzoyl derivative melted at 146-147° (from alcohol).

Found %: C 79.93, 79.99; H 6.51, 6.46; N 5.91. $C_{16}H_{15}ON$. Calculated %: C 80.30; H 6.35; N 5.92.

Deamination of p-aminophenylcyclopropane. 3 g of p-aminophenylcyclopropane was dissolved in 24 ml of dilute (1:3) hydrochloric acid, 20-25 g of ice introduced and the amine diazotized by the introduction of a solution of 1.62 g of sodium nitrite in 10 ml of water with stirring. To a solution of 4 g of sodium hydroxide in 20 ml of water was added 10 g of ice and a suspension of 1.12 g of paraformaldehyde in 4 ml of water. The mixture was stirred until the paraformaldehyde dissolved and then the solution of the diazonium salt was slowly added. The reaction mixture was stirred for 30-40 minutes and the hydrocarbon formed steam distilled. The distillate was extracted with ether; the ether extracts were washed with alkali (to remove traces of the corresponding phenol) and water and dried with calcium chloride, the ether removed and the residue distilled over sodium. The phenylcyclopropane obtained (1.5 g, 56%) had the following constants:

B. p. 172° (748 mm), n_D^{20} 1.5327, d_4^{20} 0.9418. Literature data [4]: b. p. 172.5° (745 mm), n_D^{20} 1.5336, d_4^{20} 0.9420.

The phenylcyclopropane was identified by conversion into the crystalline γ -mercurated alcohol (by reaction with mercury acetate and subsequent treatment with ammonium thiocyanate [1]), 3-hydroxy-3-phenylpropylmercury thiocyanate with m. p. 60-61° (literature data [1]: m. p. 61°); a mixed melting point of the γ -mercurated alcohol obtained with the same alcohol, synthesized from phenylcyclopropane, was not depressed.

SUMMARY

1. It was shown that nitration of phenylcyclopropane with fuming nitric acid in acetic anhydride at -50° led to the formation of p-nitrophenylcyclopropane (not described in the literature).
2. It was established that the introduction of a nitro group into the benzene nucleus of phenylcyclopropane made the three-membered ring of the latter resistant to the action of mercuric salts and also raised the resistance of the three-membered ring to oxidation.
3. Reduction of p-nitrophenylcyclopropane gave p-aminophenylcyclopropane (not described in the literature) and the structure of the latter was proved by the ultraviolet absorption spectrum, the preparation of a benzoyl derivative and also by deamination to phenylcyclopropane.

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δ-LACTONES

XVII. INTERACTION OF 5,6-DIALKYL-α-PYRONES WITH ACETYLENEDICARBOXYLIC ESTER. NEW SYNTHESIS OF 3,4-DIALKYLPHTHALIC ACIDS

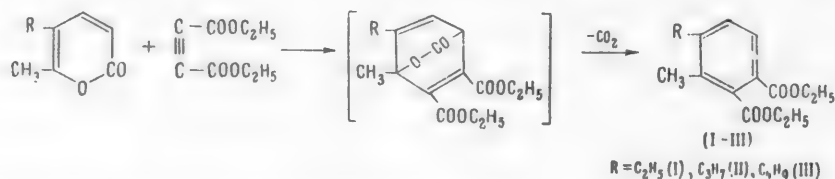
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Moscow State University

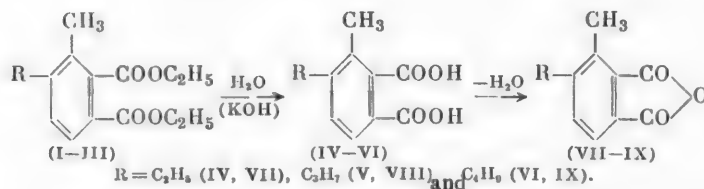
Alder and Rickert [1] were the first to study the interaction of α-pyrones with acetylenedicarboxylic ester, using as examples coumalinic and isodehydroacetic esters; the authors showed that the reaction was accompanied by the evolution of carbon dioxide and gave esters of benzenetricarboxylic acids. The application of this reaction was limited to this work, probably as a result of the inaccessibility of α-pyrones.

The new synthesis of α-pyrones we developed, consisting of the bromination of δ-enol lactones and elimination of hydrogen bromide from the dibromides formed (by distilling them), made accessible previously unknown 5,6-disubstituted α-pyrones of various structures: bi- and tricyclic α-pyrones of a condensed type [2,3], aryl- and aralkyl-α-pyrones [4, 5] and 5,6-dialkyl-α-pyrones [6].

In this work we studied the diene synthesis between acetylenedicarboxylic ester and 6-methyl-5-alkyl-α-pyrones (alkyl = ethyl, propyl and butyl), which were synthesized from the corresponding δ-enol lactones by the method described previously [6]. 5,6-Dialkyl-α-pyrones reacted with acetylenedicarboxylic ester at 130-165°; in all cases the reaction was accompanied by the evolution of carbon dioxide and gave (in good yields) esters of 3,4-dialkylphthalic acids (the esters had considerable exaltation of the molecular refraction: ~1.6-1.8).



Alkaline hydrolysis of the esters gave 3,4-dialkylphthalic acids (IV-VI) (86.75 and 93% yields) and these were sublimed to give anhydrides of 3,4-dialkylphthalic acids (VII-IX).



Thus, the reaction of 5,6-dialkyl-α-pyrones with acetylenedicarboxylic ester and hydrolysis of the adduct thus formed may be used as a method of preparing 3,4-dialkylphthalic acids. None of the substances synthesized in this work have been described in the literature.

An attempt to react α -pyrones with acetylenedicarboxylic acid did not give positive results: the acid was decarboxylated under the reaction conditions, though data are given in the literature on the successful use of acetylenedicarboxylic acid as a dienophile at even higher temperatures (170°) [7, 8].

EXPERIMENTAL

Synthesis of diethyl 3,4-dialkylphthalates (I-III). A mixture of equimolecular amounts (0.04 mole each) of the appropriate α -pyrone* and acetylene dicarboxylic ester (b. p. 107-108° at 13 mm, n_D^{20} 1.4405 [9]) was heated on an oil bath in a flask with a reflux condenser. Vigorous evolution of carbon dioxide began at 130-165°; after 20-30 minutes, when the evolution of gas became less vigorous, the temperature was raised to 180-190°; heating at this temperature was continued for 1-2 hours until the evolution of carbon dioxide ceased completely (the gas liberated represented 75-95% of the calculated volume in all experiments) and the reaction mixture was then vacuum distilled.

Diethyl 3-methyl-4-ethylphthalate (I). Yield 73%.

B. p. 148-150° at 6.5 mm, n_D^{20} 1.5110, d_4^{20} 1.0847, MR_D 72.98. $C_{15}H_{20}O_4$. Calculated 71.17; EM_D 1.81.

Found %: C 68.40, 68.21; H 7.86; 7.68. $C_{15}H_{20}O_4$. Calculated %: C 68.15; H 7.63.

Diethyl 3-methyl-4-propylphthalate (II). Yield 90%.

B. p. 138-139° at 3.5 mm, n_D^{20} 1.5070, d_4^{20} 1.0660, MR_D 77.66. $C_{16}H_{22}O_4$. Calculated 75.79; EM_D 1.87.

Found %: C 69.34, 69.39; H 8.07, 8.22. $C_{16}H_{22}O_4$. Calculated %: C 69.04; H 7.97.

Diethyl 3-methyl-4-butylphthalate (III). Yield 75%.

B. p. 164-165° at 3.5 mm, n_D^{20} 1.5048, d_4^{20} 1.0560, MR_D 82.06. $C_{17}H_{24}O_4$. Calculated 80.41; EM_D 1.65.

Found %: C 69.78, 69.58; H 8.05, 7.98. $C_{17}H_{24}O_4$. Calculated %: C 69.80; H 8.12.

Preparation of 3,4-dialkylphthalic acids (IV-VI) and their anhydrides (VII-IX). 7 g of the dialkylphthalic ester and 35 ml of a 20% alcohol solution of potassium hydroxide was boiled for 2 hours; crystalline salts precipitated from solution. Water (20 ml) was added to dissolve the precipitate and the reaction mixture boiled for a further 1 hour. After removal of the alcohol, the residue was acidified with concentrated hydrochloric acid; the precipitated crystals of dialkylphthalic acid were recrystallized from water and dried in a vacuum desiccator over sulfuric acid.

3-Methyl-4-ethylphthalic acid (IV). The yield was 86% and the m. p. 151-152°

Found %: C 63.98, 64.00; H 5.94, 5.99. $C_{11}H_{12}O_4$. Calculated %: C 63.45; H 5.81.

3-Methyl-4-propylphthalic acid (V). The yield was 75% and the m. p. 154-155°.

Found %: C 64.60, 64.47; H 6.51, 6.60. $C_{12}H_{14}O_4$. Calculated %: C 64.85; H 6.35.

3-Methyl-4-butylphthalic acid (VI). The yield was 93% and the m. p. 157-158°.

Found %: C 66.56, 66.41; H 7.18, 7.03. $C_{13}H_{16}O_4$. Calculated %: 66.08; H 6.83.

Slow sublimation of the dialkylphthalic acids (IV-VI) yielded their anhydrides (VII-IX).

3-Methyl-4-ethylphthalic anhydride (VII). The yield was 88% and the m. p. 67-68°.

Found %: C 69.80, 70.01; H 5.67, 5.62. $C_{11}H_{10}O_3$. Calculated %: C 69.45; H 5.34.

3-Methyl-4-propylphthalic anhydride (VIII). The yield was 81% and the m. p. 74-75°.

Found %: C 70.70, 70.95; H 5.87, 5.96. $C_{12}H_{12}O_3$. Calculated %: C 70.60; H 5.90.

* The starting α -pyrones [6] had the following constants: 6-methyl-5-ethyl- α -pyrone - b. p. 121-123° at 7 mm, n_D^{20} 1.5182, d_4^{20} 1.0780; 6-methyl-5-propyl- α -pyrone - b. p. 120-121° at 6 mm, n_D^{20} 1.5170, d_4^{20} 1.0515; 6-methyl-5-butyl- α -pyrone - b. p. 119-121° at 3 mm, n_D^{20} 1.5128, d_4^{20} 1.0275.

3-Methyl-4-butylphthalic anhydride (IX). The yield was 91% and the m. p. 37°.

Found %: C 71.25, 71.35; H 6.66, 6.64. $C_{13}H_{14}O_3$. Calculated %: C 71.53; H 6.46.

SUMMARY

1. Reaction of 5,6-dialkyl- α -pyrones with acetylenedicarboxylic ester followed by hydrolysis of the adduct thus obtained may be used as a method for preparing 3,4-dialkylphthalic esters and the corresponding phthalic acids.

2. By this method we synthesized the diethyl esters of 3-methyl-4-ethyl-3-methyl-4-propyl- and 3-methyl-4-butylphthalic acids and the corresponding acids and anhydrides that have not been described previously.

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CHEMISTRY OF SELENOPHENE

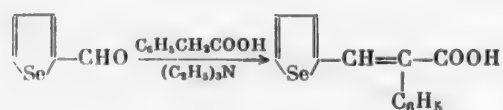
XX. CONDENSATION OF SELENOPHENE-2-ALDEHYDE WITH ESTERS OF SUBSTITUTED ACETIC ACIDS AND NITROMETHANE

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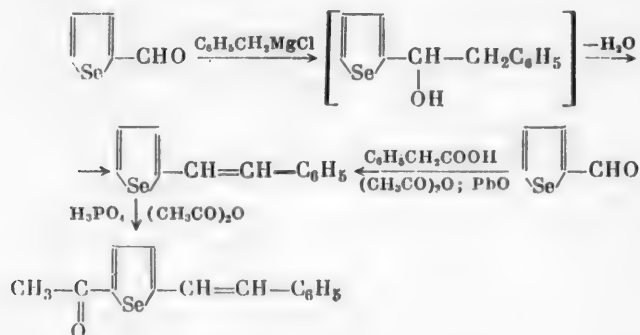
In the present work, continuing our study of the reactions of selenophene-2-aldehyde [1-5], we investigated its condensations with compounds containing active methylene groups (phenylacetic acid, methyl and ethyl acetates and nitromethane) and also its behavior in the Darzan and Leicart reactions.

The interaction of selenophene-2-aldehyde with phenylacetic acid in the presence of triethylamine yielded α -phenyl- β -(selenienyl-2)-acrylic acid.

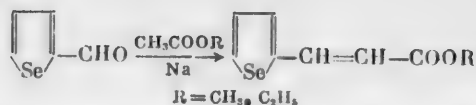


If this condensation was carried out in acetic anhydride in the presence of lead oxide, decarboxylation occurred and α -phenyl- β -(selenienyl-2)-ethylene was formed. We also synthesized the latter by the interaction of benzylmagnesium chloride with selenophene-2-aldehyde with subsequent dehydration of the carbinol formed.

By acylation of α -phenyl- β -(selenienyl-2)-ethylene with acetic anhydride in the presence of phosphoric acid we obtained α -phenyl- β -(5-acetoselenienyl-2)-ethylene.

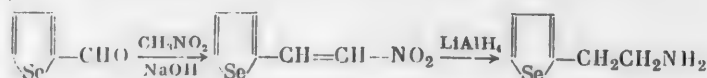


Condensation of selenophene-2-aldehyde with methyl and ethyl acetates in the presence of sodium led to the corresponding esters of β -(selenienyl-2)-acrylic acid.



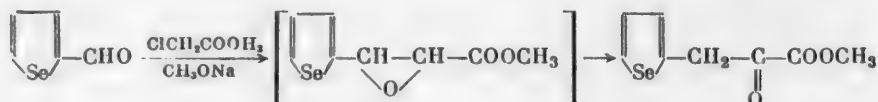
An attempt to prepare β -(selenienyl-2)-acrylonitrile by the interaction of selenophene-2-aldehyde with acetonitrile was unsuccessful: the condensation did not occur under the action of alkali or metallic sodium or catalytically (in the presence of sodium acetate on silica gel at 300-400°).

By the interaction of selenophene-2-aldehyde with nitromethane we obtained ω -nitrovinylselenophene and reduction of this with lithium aluminum hydride gave β -(selenienyl-2)-ethylamine.



An attempted Leicart reaction with selenophene-2-aldehyde under normal and more drastic conditions was unsuccessful and the aldehyde was recovered unchanged.

By condensation of selenophene-2-aldehyde with methyl monochloroacetate in the presence of sodium methylate under the conditions of the Darzan reaction [6] and vacuum distillation of the condensation product we obtained the methyl ester of selenienyl-2-pyruvic acid, formed by isomerization of the β -(selenienyl-2)-glycidic ester formed.



A similar thermal isomerization of a glycidic ester has been described in the literature for β, β -diphenylglycidic ester, which rearranged into diphenylpyruvic ester when vacuum distilled [7, 8].

EXPERIMENTAL

α -Phenyl- β -(selenienyl-2)-acrylic acid. 7 g (0.044 mole) of selenophene-2-aldehyde, 7.5 g (0.055 mole) of phenylacetic acid, 5 ml of triethylamine and 10 ml of acetic anhydride were boiled gently for 4 hours. After removal of the unchanged phenylacetic acid by steam distillation, the solid residue was dissolved in 120 ml of methyl alcohol and boiled with charcoal. After filtration, the hot filtrate was made acid with 2 N hydrochloric acid and diluted with 100 ml of water. We obtained 9.1 g (74%) of product. The m. p. was 185-186° (from 60% methyl alcohol).

Found %: C 56.42, 56.58; H 4.01, 3.86. $\text{C}_{12}\text{H}_{10}\text{O}_2\text{Se}$. Calculated %: C 56.33; H 3.64.

Methyl β -(selenienyl-2)-acrylate. To 30 g (0.40 mole) of absolute methyl acetate and 1.85 g (0.08 g-at.) of sodium were added a few drops of anhydrous alcohol and with vigorous stirring at 5-10° 10 g (0.063 mole) of selenophene-2-aldehyde was added over 15 minutes. The mixture was stirred for a further hour and then 6 ml of concentrated hydrochloric acid in 20 ml of water added. After the upper layer had been separated, the aqueous one was extracted with ethyl acetate, the combined extracts were washed with dilute hydrochloric acid and water and dried with magnesium sulfate. After removal of the solvent in vacuum, the residue was distilled at 113-115° (25 mm); the light yellow oil crystallized on cooling. We obtained 8.7 g (64.5%) of product with m. p. 36-37° (from ligroine).

Found %: C 45.05, 44.95; H 3.89, 3.91. $\text{C}_9\text{H}_8\text{O}_2\text{Se}$. Calculated %: C 44.66; H 3.75.

Ethyl β -(selenienyl-2)-acrylate. Using the above procedure, we obtained 17 g (74%) of product from 16 g (0.1 mole) of selenophene-2-aldehyde, 50 g (0.67 mole) of absolute ethyl acetate and 3 g (0.13 g-at.) of sodium.

B. p. 115-116° (15 mm), n_D^{20} 1.6157, d_4^{20} 1.4239, M_R 56.23. $\text{C}_9\text{H}_{10}\text{O}_2\text{Se}$. Calculated 52.46.

Found %: C 46.59, 46.86; H 4.19, 4.54. $\text{C}_9\text{H}_{10}\text{O}_2\text{Se}$. Calculated %: C 47.02; H 4.35.

ω -Nitrovinylselenophene. A solution of 5.4 g (0.135 mole) of sodium hydroxide in 20 ml of water was added to 20 g (0.125 mole) of selenophene-2-aldehyde and 8 g (0.13 mole) of nitromethane in 25 ml of methyl alcohol at 5-8° with stirring (temperature no higher than 10-15°). The mixture was stirred for a further 30 minutes and dissolved in 100 ml of water and this solution was rapidly added dropwise with vigorous stirring to a mixture of 25 ml of concentrated hydrochloric acid and 50 g of ice. The precipitate was washed with ice water, dissolved in methyl alcohol and boiled with charcoal. We obtained 15.5 g (61%) of product with m. p. 67-68° (from methyl alcohol); it was volatile and irritated the mucous membranes of the nasopharynx and the skin.

Found %: C 36.08, 37.17; H 2.67, 2.69. $C_6H_5O_2NSe$. Calculated %: C 35.66; H 2.49.

β -(Selenienyl-2)-ethylamine. A solution of 10 g (0.049 mole) of ω -nitrovinylselenophene in 200 ml of absolute ether was added with stirring to a solution of lithium aluminum hydride [from 8 g (1.0 mole) of lithium hydride and 45.1 g (0.19 mole) of aluminum bromide] in 300 ml of absolute ether at such a rate that the ether boiled gently; the mixture was heated for 2 hours on a water bath and cooled and to it was added 20 ml of water and then 10 ml of 40% sodium hydroxide solution. The ether layer was separated and the aqueous one steam distilled and the distillate extracted with ether. The combined ether extracts were dried with potassium carbonate and, after removal of the ether, the residue vacuum distilled. We obtained 6.1 g (75%) of product.

B. p. 120-121° (11 mm), n_D^{20} 1.5856, d_4^{20} 1.4571, MR_D 40.06. $C_6H_9NSeF_2$. Calculated 40.85.

Found %: C 41.86, 41.75; H 5.49, 5.35. C_6H_9NSe . Calculated %: C 41.39; H 5.21.

α -Phenyl- β -(selenienyl-2)-ethylene. a) A solution of 10 g (0.06 mole) of selenophene-2-aldehyde in 50 ml of absolute ether was added with stirring to a solution of benzylmagnesium chloride from 12.5 g (0.08 mole) of benzyl chloride and 2.43 g (0.1 g-at.) of magnesium in 50 ml of absolute ether. The mixture was heated on a water bath for 2 hours and decomposed with acetic acid. The ether layer was separated and the aqueous one extracted with ether. The ether was removed; to the residue was added 3 ml of acetic acid and the mixture boiled for 20 minutes, poured into 200 ml of water and extracted with ether. The ether extracts were washed with potassium carbonate solution and dried with calcium chloride. After removal of the ether, the residue was vacuum distilled at 140-145° (2 mm). We obtained 9 g (61%) of product with m. p. 128-129° (from methyl alcohol).

b) A mixture of 8 g (0.05 mole) of selenophene-2-aldehyde, 8 g (0.059 mole) of phenylacetic acid, 5 g of lead oxide and 15 ml of acetic anhydride was boiled for 5 hours and cooled and to it was added 50 ml of water. The precipitate was washed with aqueous methyl alcohol, dissolved in 150 ml of methyl alcohol and boiled with charcoal. We obtained 4.1 g (35%) of product with m. p. 128-129° (from methyl alcohol). A mixed melting point with α -phenyl- β -(selenienyl-2)-ethylene, obtained by method "a", was not depressed (m. p. 128-128.5°).

Found %: C 61.93, 61.91; H 4.47, 4.56. $C_{12}H_{10}Se$. Calculated %: C 61.81; H 4.29.

α -Phenyl- β -(5-acetoselenienyl-2)-ethylene. A mixture of 0.55 g of 85% phosphoric acid and 2.5 g of acetic anhydride, prepared the day before, was added with stirring and water cooling to a solution of 10 g (0.043 mole) of α -phenyl- β -(selenienyl-2)-ethylene and 2.6 g (0.025 mole) of acetic anhydride in 100 ml of benzene. The mixture was heated at 70-75° for 1 hour and then the benzene removed by steam distillation. We obtained 2 g (17%) of product with m. p. 135-136° (from methyl alcohol).

Found %: C 61.23, 61.11; H 4.47, 4.56. $C_{14}H_{12}OSe$. Calculated %: C 61.09; H 4.39.

Methyl (selenienyl-2)-pyruvate. In a three-necked flask with a stirrer, 8.1 g (0.15 mole) of sodium methylate was suspended in 100 ml of absolute ether and a solution of 16 g (0.1 mole) of selenophene-2-aldehyde and 16.3 g (0.15 mole) of methyl chloroacetate in 50 ml of ether added dropwise with stirring and cooling in water. The mixture was left for 12 hours, heated on a water bath for 30 minutes, poured onto ice (~100 g) and acidified with acetic acid. The ether layer was separated and the aqueous one extracted with ether. The ether extracts were washed with water and dried with anhydrous magnesium sulfate. After removal of the ether, the residue was vacuum distilled to yield 12.1 g (52.5%) of product with b. p. 149-151° (3-4 mm) and m. p. 72-73° (from heptane).

Found %: C 41.78, 41.62; H 3.72, 3.71. $C_8H_8O_3Se$. Calculated %: C 41.57; H 3.49.

The thiosemicarbazone of methyl (selenienyl-2)-pyruvate was prepared from 0.1 g of ester, 0.1 g of thiosemicarbazide hydrochloride and 0.15 g of sodium acetate; it had m. p. 194-195° (from alcohol).

Found %: Se 25.88, 25.80. $C_9H_{11}O_2NSSe$. Calculated %: Se 25.96.

SUMMARY

1. Condensation of selenophene-2-aldehyde with phenylacetic acid and methyl and ethyl acetates led to the formation of either α -phenyl- β -(selenienyl-2)-acrylic acid or α -phenyl- β -(selenienyl-2)-ethylene and methyl and ethyl β -(selenienyl-2)-acrylates, respectively.

2. Condensation of selenophene-2-aldehyde with nitromethane led to the formation of ω -nitrovinylselenophene and reduction of the latter gave β -(selenienyl-2)-ethylamine.

3. The interaction of selenophene-2-aldehyde with methyl monochloroacetate under the conditions of the Darzan reaction led to methyl (selenienyl-2-)-pyruvate.

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CATALYTIC ALKYLATION OF BENZENE AND TOLUENE WITH PROPYL ALCOHOLS

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In continuing a study of the effect of substituents in the benzene ring on the course of an alkylation reaction, in the present work we studied the conditions for the alkylation of benzene and toluene by propyl alcohols.

As is known, at the present time isopropylbenzene and isopropyltoluene are raw materials which are widely used in the chemical industry [1, 2].

For studying the alkylation, we used home-produced industrial aluminosilicate catalyst. We previously alkylated benzene with propyl alcohols on imported Gudri catalyst [3]. So as to be able to compare the results of the alkylation of benzene and toluene, we repeated the alkylation of benzene on home-produced catalyst.

As in previous work, in the present investigation the alkylation was at atmospheric pressure. We examined the effect of temperature, rate of reaction mixture input and molar ratios of components and the effect of the structure of the alcohols on the yield of alkylation products.

The alkylation of benzene and toluene with *n*-propyl alcohol led to alkylation products with an *iso*-structure and the yields were 12-15% lower than those when isopropyl alcohol was used.

The yield of alkylation products mainly depended on the concentration of hydrocarbons in the reaction mixture. When the hydrocarbon concentration was raised from 2 to 6 moles at the optimal temperature (250°) and a

volume rate of 0.2 hours⁻¹, the yield of isopropylbenzene rose from 29 to 56% and that of isopropyltoluene, from 39 to 74%. A further increase in the hydrocarbon concentration had less effect on the yield of alkylation products. At a ratio of 20 moles of hydrocarbon to 1 mole of alcohol, the yield of isopropylbenzene reached 73.5% and that of isopropyltoluene, 79.5%. By re-use of the excess unreacted hydrocarbon, we were able to raise the yield of isopropylbenzene to 96% and that of isopropyltoluene to 98%. In a previous paper [4], we explained the increase in the yields of alkyl-substituted benzenes under these conditions by the presence of small amounts (about 0.12%) of propylene polymers in the unreacted hydrocarbons.

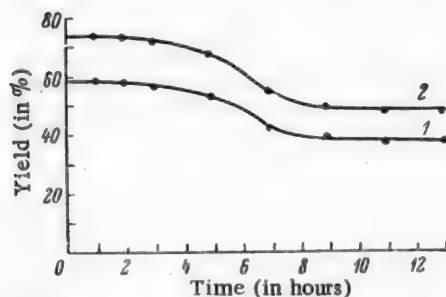


Fig. 1. Dependence of alkylation product yield on duration of action of catalyst. 1) Benzene, 2) toluene.

isomer: the *ortho*-isomer could not be detected. The presence of *m*-isopropyltoluene in the alkylation products formally contradicts the orientation rule, but agrees with experimental facts on the predominance of the *meta*-orienting effect of an alkyl group in alkylation reactions [5-11].

EXPERIMENTAL

The starting materials, which were first purified and distilled, had constants agreeing with literature data.

The reaction was performed over 100 ml of industrial aluminosilicate catalyst balls with a bulk weight of 0.817 in a normal apparatus for catalytic reactions in a flow system [1]. The catalyst was first fired for 3 hours in a stream of dry air at 500°. The catalyst was regenerated under the same conditions after each experiment and then it had the original appearance and activity. About 50 ml of a mixture of reagents was used for each experiment. At the end of each experiment, the catalyzate was flushed out with a weak stream of nitrogen for 30 minutes.

The products from the alkylation of benzene* with isopropyl alcohol were collected over the range of 150-154° and with n-propyl alcohol, 150-161°; the products from the alkylation of toluene with propyl alcohols were collected over the range 172-180°. The yield of alkylation products (fractions corresponding only to

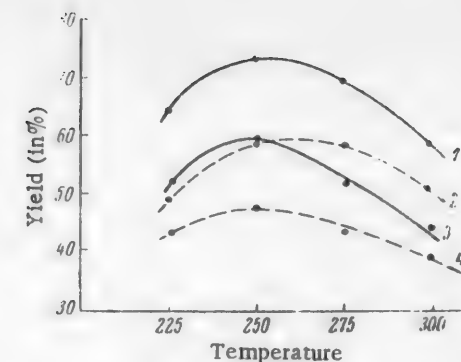


Fig. 2. Dependence of alkylation product yield on temperature. 1) Yield of isopropyltoluene in alkylation with isopropyl alcohol, 2) yield of isopropylbenzene in alkylation with isopropyl alcohol, 3) yield of isopropyltoluene in alkylation with n-propyl alcohol, 4) yield of isopropylbenzene in alkylation with n-propyl alcohol.

monoalkyl products) was calculated on the alcohol reacting. The amount of disubstituted products formed was small and they were not investigated in detail.

The duration of action of the catalyst was studied in the alkylation of benzene and toluene with isopropyl alcohol at 250° with a reagent input volume rate of 0.2 hours⁻¹ and a molar ratio of 6:1. During the first 3 hours the catalyzate was collected every hour and then every 2 hours; after 13 hours, when the activity of the catalyst had fallen noticeably, it was regenerated and recovered its activity completely. The results of this series of experiments are presented in Fig. 1.

The determination of the optimal temperature for the alkylation of benzene and toluene was carried out over the range 225-300° at a molar ratio of hydrocarbon to alcohol of 6:1 and a reaction mixture input volume rate of 0.2 hours⁻¹. The results of the experiments are presented in Fig. 2. By separate experiments it was shown that the optimal temperature remained the same, namely 250°, at other molar ratios of reagents.

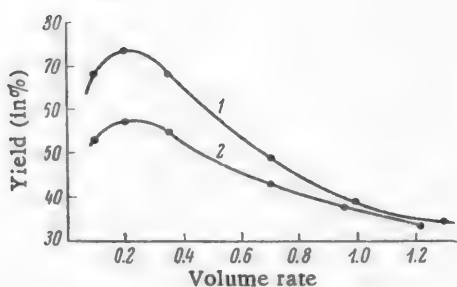


Fig. 3. Dependence of alkylation product yield on reaction mixture input rate. 1) Yield of isopropyltoluene, 2) yield of isopropylbenzene.

The effect of the reaction mixture input rate on the yield of isopropylbenzene and isopropyltoluene was studied only with mixtures of hydrocarbons and isopropyl alcohol in a ratio of 6:1 at 250°. The volume rates were varied from 0.1 to 1.2 hours⁻¹. The results of the experiments are presented in Fig. 3.

The effect of the starting mixture composition on the yield of isopropylbenzene and isopropyltoluene was studied at 250° and a reaction mixture input volume rate of 0.2 hours⁻¹. The molar ratio of the reaction mixture components was varied from 2:1 to 20:1. Pure hydrocarbons were used in one series of experiments and the excesses distilled from previous experiments, in the other (Fig. 4). In the case of benzene, this fraction boiled at 65-85°; in the case of toluene it boiled at 65-112°. Like the whole catalyzate, these fractions had an unsaturated character.

To obtain pure hydrocarbons, fractions of isopropylbenzene and isopropyltoluene were isolated from the preliminarily dried catalyzates by distillation from a Favorskii flask and these were shown to contain 0.16-0.17% of unsaturated compounds by titration by Kaufmann's method. To remove these compounds, the fractions investigated

* The benzene had to be freed from thiophene for the catalyst to retain its activity for a long period.

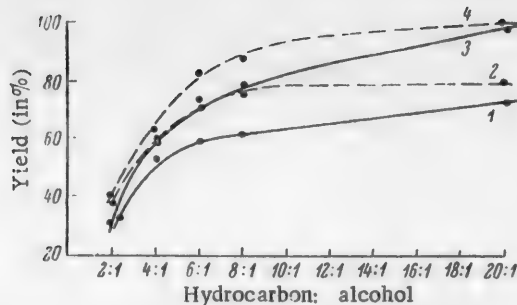


Fig. 4. Dependence of alkylation product yield on reagent ratio. 1) Yield of isopropylbenzene in alkylation of pure hydrocarbon, 2) yield of isopropyltoluene in alkylation of pure hydrocarbon, 3) yield of isopropylbenzene in alkylation of excess unreacted hydrocarbon, 4) yield of isopropyltoluene in alkylation of excess unreacted hydrocarbon.

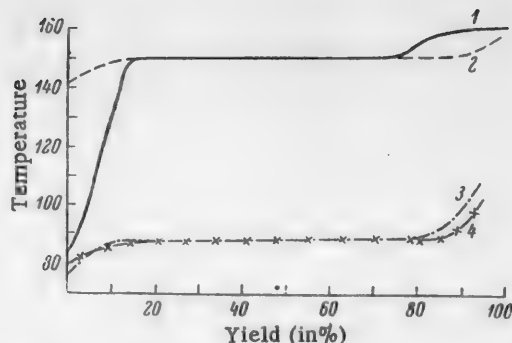


Fig. 5. Distillation curves. 1) Isopropylbenzene: fraction obtained by alkylation with isopropyl alcohol; 2) isopropylbenzene fraction obtained by alkylation with n-propyl alcohol; 3) isopropyltoluene fraction obtained by alkylation with isopropyl alcohol; 4) isopropyltoluene fraction obtained by alkylation with n-propyl alcohol.

were treated with Kaufmann's bromine mixture and then, after appropriate purification, distilled on a column with a metal packing and an efficiency of 70 theoretical plates.

The results of distilling the isopropylbenzene fractions (150-154° and 150-161°) are presented in Fig. 5. The isopropylbenzene isolated in both series of experiments had the following constants:

B. p. 151.5-151.9° (750 mm), n_D^{20} 1.4919, d_4^{20} 0.8624; literature data [12]: b. p. 152.4° (760 mm), n_D^{20} 1.4915, d_4^{20} 0.8618; n-propylbenzene has b. p. 159.2°, n_D^{20} 1.4920, d_4^{20} 0.8620.

The starting benzene and the isopropylbenzene obtained did not undergo any changes when passed over the catalyst at 250° and a volume rate of 0.2 hours⁻¹. Under these conditions, isopropyl alcohol was 96-97% dehydrogenated. Apart from propylene, a mixture of hydrocarbons with b. p. 69-200°, representing 3-4% of the alcohol introduced, was obtained. No ether was detected in the catalyzate.

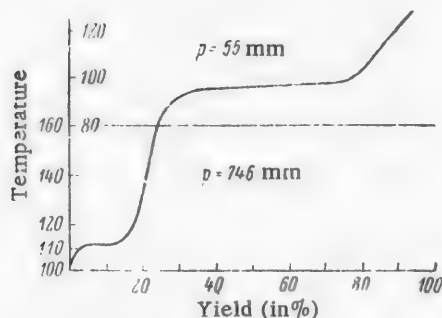


Fig. 6. Distillation curve of isopropyltoluene cracking products.

The results of distilling the isopropyltoluene fractions (172-180°) are presented in Fig. 5. The isopropyltoluene had the following constants:

B. p. 89.0-89.2° (45 mm), n_D^{20} 1.4931, d_4^{20} 0.8614; literature data [12]: o-isopropyltoluene: b. p. 178.15°, n_D^{20} 1.5600, d_4^{20} 0.8766; m-isopropyltoluene: b. p. 175.14°, n_D^{20} 1.4930, d_4^{20} 0.8610, n-isopropyltoluene: b. p. 177.10°, n_D^{20} 1.4909, d_4^{20} 0.8573.

When the isopropyltoluene obtained was passed over the catalyst at 250° with a volume rate of 0.2 hours⁻¹, a catalyzate was obtained, from which 10% of toluene was isolated (Fig. 6).

The isopropyltoluene was identified by oxidation with dilute nitric acid by the procedure in [13] with subsequent esterification and isolation of the esters by the procedure in [14]. Many recrystallizations of the esters from dilute alcohol yielded dimethyl isophthalate with m. p. 63° and dimethyl terephthalate with m. p. 139°. According to Moldavskii's data, dimethyl isophthalate melts at 65-66° and dimethyl terephthalate at 139°. No ortho-isomer was detected in any case.

The alkylation product was analyzed spectrally. The intensity of the lines was measured visually relative to the line at 1610 cm⁻¹, whose intensity was arbitrarily taken as 10 units.

Spectrum of toluene alkylation product: 224 (4), 306 (4) 442 (1), 524 (3), 556 (0.5), 587 (0), 644 (2.5), 710 (6), 803 (4.5), 822 (2), 956 (1), 998 (30), 1068 (1.5), 1104 (2), 1187 (1), 1207 (5), 1246 (2), 1270 (1), 1304 (1.5), 1382 (4), 1443 (3, broad), 1460 (3, broad), 1593 (0), 1610 (10).

From a comparison of the spectrum obtained with the Raman spectra of methylisopropylbenzenes given in the literature [15], it follows that the product from the alkylation of toluene with isopropyl alcohols was a mixture of meta- and para-isomers, 63 and 37%, respectively.

SUMMARY

1. Benzene and toluene were alkylated with propyl alcohols in a catalytic system of the flow type over an aluminosilicate catalyst at atmospheric pressure.

2. The optimal conditions for preparing isopropylbenzene and isopropyltoluene (para- and meta-isomers) were found to be 250° and a reaction mixture input volume rate of 0.2 hours⁻¹. At a ratio of 20 moles of hydrocarbon to 1 mole of alcohol, the yield of isopropylbenzene was 96% and that of isopropyltoluene, 98%.

3. Alkylation of benzene and toluene with n-propyl alcohol led to compounds of iso-structure in yields which were 12-15% lower than those obtained in alkylations with isopropyl alcohol.

4. With periodic regeneration, the catalyst retained its original activity after 500 hours operation.

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ABSORPTION SPECTRA OF DISUBSTITUTED BENZENES WITH SIMILARLY DIRECTING FUNCTIONAL GROUPS

II. ABSORPTION SPECTRA OF NITROBENZALDEHYDES

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The absorption spectra of nitrobenzaldehydes are of interest in connection with the elucidation of the nature of electron transitions, connected with separate absorption bands of substituted aromatic compounds [1, 2], and also in connection with a study of the effect on absorption of the intramolecular hydrogen bond, involving the hydrogen of the aldehyde group, proposed for ortho-nitrobenzaldehyde on the basis of the chemical behavior of the latter [3] and the value of the oscillation frequencies of the carbonyl group [4]. The absorption spectra of the compounds examined have been measured in hydrocarbons and alcohols [5-9]. We measured them in hexane, benzene, dioxane, diethyl ether, n-butanol and concentrated (98%) and dilute aqueous sulfuric acid (9.8%).

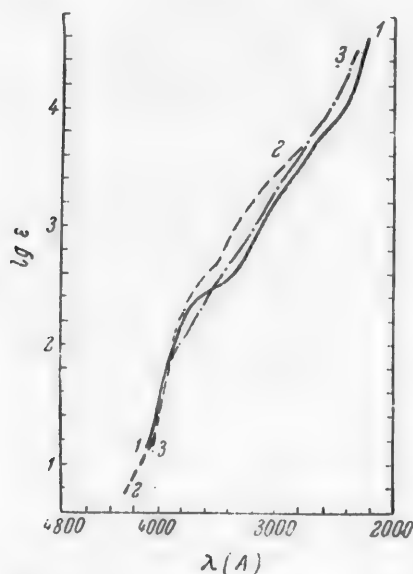


Fig. 1. o-Nitrobenzaldehyde in non-polar solvents. 1) In hexane ($5 \cdot 10^{-3}$ – $5 \cdot 10^{-5}$ M), 2) in benzene ($2 \cdot 10^{-2}$ – $2 \cdot 10^{-4}$ M), 3) in dioxane ($2 \cdot 10^{-2}$ – $4 \cdot 10^{-5}$ M).

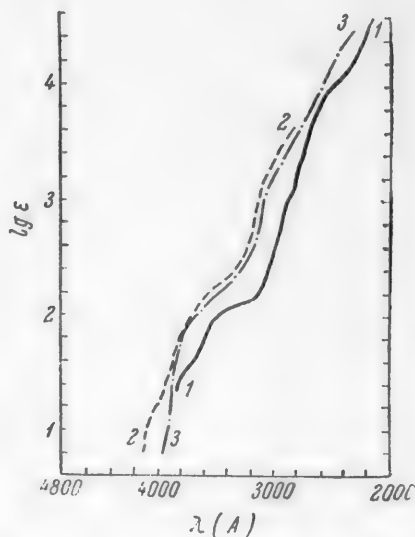


Fig. 2. m-Nitrobenzaldehyde in non-polar solvents. 1) In hexane ($5 \cdot 10^{-3}$ – $5 \cdot 10^{-5}$ M), 2) in benzene ($2 \cdot 10^{-2}$ – $2 \cdot 10^{-4}$ M), 3) in dioxane ($2 \cdot 10^{-2}$ – $2 \cdot 10^{-5}$ M).

The absorption curves of nitrobenzaldehydes in nonpolar solvents (Figs. 1-3) were found to be identical to each other and also to that of nitrobenzene (see Table) with respect to number and position of absorption bands.

Only with *para*-nitrobenzaldehyde was there an noticeable shift in the curve toward longer wavelengths (including the maximum of band B), together with an increase in the oscillation strength and half-width ($b/2$) of band B. The absorption curves of nitrobenzaldehydes in hexane almost coincided with those of nitroacetophenones [2]. Only with *o*-nitrobenzaldehyde was the absorption curve up to $\lg \epsilon \approx 2.4$ slightly displaced toward longer and above $\lg \epsilon \approx 2.4$, toward shorter wavelengths in comparison with *o*-nitroacetophenone.

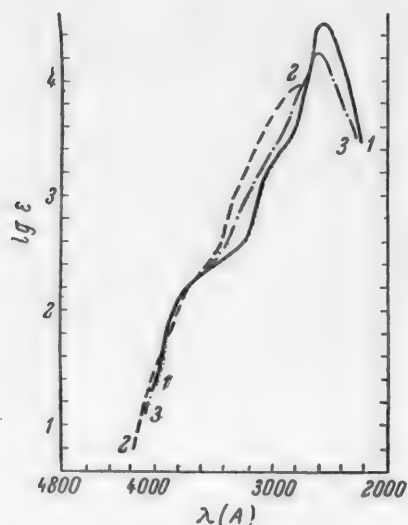


Fig. 3. *p*-Nitrobenzaldehyde in non-polar solvents. 1) In hexane ($2 \cdot 10^{-3}$ – $5 \cdot 10^{-5}$ M), 2) in benzene ($5 \cdot 10^{-3}$ – $5 \cdot 10^{-5}$ M), 3) in dioxane ($2 \cdot 10^{-2}$ – $2 \cdot 10^{-5}$ M).

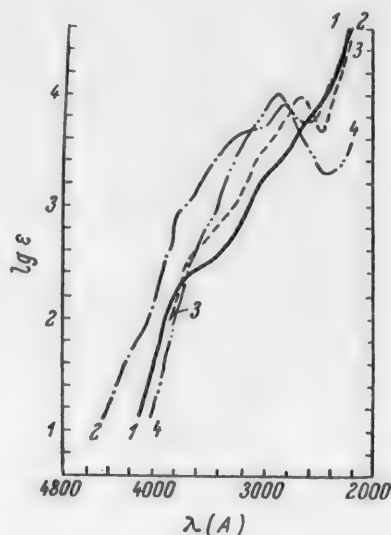


Fig. 4. *o*-Nitrobenzaldehyde in sulfuric acid. 1) In hexane, 2) in 98% sulfuric acid ($2 \cdot 10^{-2}$ – $2 \cdot 10^{-5}$ M), 3) in 9.8% sulfuric acid, 4) nitrobenzene in 98% sulfuric acid ($2 \cdot 10^{-2}$ – $2 \cdot 10^{-4}$ M).

In benzene and dioxane, as compared with hexane, there was a slight shift in the absorption curves of all nitrobenzaldehydes (apart from the *ortho*- and *para*-isomers below $\lg \epsilon \approx 2.0$ – 2.2) toward longer wavelengths. The same (but to a lesser extent with the *ortho*-isomer) was also observed in diethyl ether and butanol (see Table).

In concentrated sulfuric acid (Figs. 4–6) the absorption curves of all the nitrobenzaldehydes underwent a considerable shift toward longer wavelengths, as is also observed for nitroacetophenones and unsubstituted nitrobenzene and benzaldehyde. This shift was especially marked for the maximum of band B; according to the magnitude of the shift (for the value of $\Delta E = E_{\text{hexane}} - E_{\text{conc. H}_2\text{SO}_4}$ see Table) the isomers may be arranged in the series $o > m > p$.

In contrast to nitroacetophenones, not only *p*-, but also *o*-nitrobenzaldehyde showed a considerable shift toward longer wavelengths in comparison with the curve of nitrobenzene in concentrated sulfuric acid; the curve of *m*-nitrobenzaldehyde, like that of *m*-nitroacetophenone was noticeably displaced toward shorter wavelengths in comparison with that of nitrobenzene in concentrated sulfuric acid. In 9.8% acid the absorption curves of nitrobenzaldehydes were to a considerable extent restored to those in such solvents as benzene and dioxane.

The character of the absorption of nitrobenzaldehydes reported above may be explained qualitatively, as in the case of nitroacetophenones [2], with the premise that the longwave inflection is connected with $p \rightarrow \pi^*$ electron transitions in the nitro group and the band B, with $N \rightarrow \nu$ transitions, leading to the formation of intramolecularly ionized structures in an excited state [10, 11]. The similarity of the curves (in position and number of bands and in the change with the nature of the solvent) of isomeric nitrobenzaldehydes to each other and that of nitrobenzene indicates that under the action of the electric field of a light wave, in the molecules of these substances there may occur displacements of charges in different directions with the formation of different intramolecularly ionized structures in an excited state.

Intramolecularly ionized structures of this type presupposes a higher stability in the excited than in the ground state for the intermolecular hydrogen bond in hydroxyl-containing solvents and for the oxonium compound in concentrated acids. This makes it possible to explain [12] the shift of band B toward longer wavelengths in these media. A certain shift in the longwave inflection in the same direction in concentrated sulfuric acid presupposes that the absorption bands, connected with $p \rightarrow \pi^*$ transitions in complex groups, containing several pairs of p - and π -electrons, involved in conjugation with the π -electron system of the ring, do not essentially have the same characteristics [13, 14] as the bands of the same type of transition of groups containing only one pair of free electrons, as with the nitrogen of amino and imino groups.

Absorption Characteristics of Nitrobenzaldehydes

Compound	Band B in hexane				$\Delta E = E_{\text{hexane}} - E_{\text{butanol}}$ (in kcal/mole)	$\Delta E = E_{\text{hexane}} - E_{\text{conc. H}_2\text{SO}_4}$ (in kcal/mole)
	$h\nu$ of maximum (in eV)	f_e	half-width $b/2$ at $\lg \epsilon$ 3.8 (in Å)	$\frac{\epsilon_{\text{nitrobenzaldehyde}}}{\epsilon_{\text{nitrobenzene}}}$		
Nitrobenzene	4.87	0.22	115	—	+7.6	+16.9
Benzaldehyde	(5.14)[10]	(0.27)[10]	—	—	—	—
Nitrobenzaldehyde	o 4.97 (inflection)	—	—	~1.0	~-0.9	+15.5
	m 4.83 (inflection)	—	—	~1.0	~+4.3	+7.5
	p 4.67	0.58	230	3.1	+1.8	+6.8

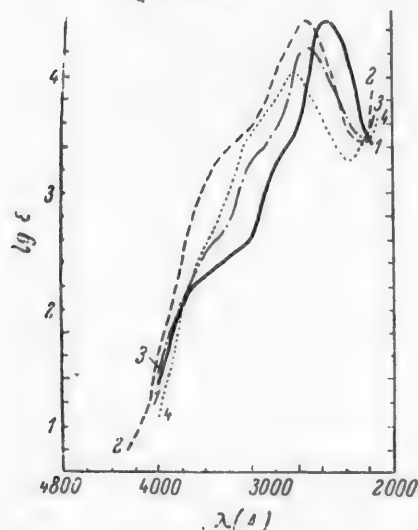


Fig. 5. *p*-Nitrobenzaldehyde in sulfuric acid. 1) In hexane, 2) in 98% sulfuric acid, 3) in 9.8% sulfuric acid, 4) nitrobenzene in 98% sulfuric acid.

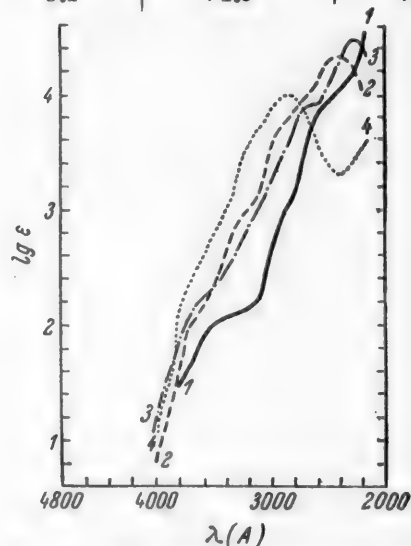


Fig. 6. *m*-Nitrobenzaldehyde in sulfuric acid. 1) In hexane, 2) in 98% sulfuric acid, 3) in 9.8% sulfuric acid, 4) nitrobenzene in 98% sulfuric acid.

As was established above, in contrast to its isomers, o-nitrobenzaldehyde shows a series of peculiarities as regards the absorption of light, in comparison with o-nitroacetophenone. However, these peculiarities are not essentially connected with the presence of an intramolecular hydrogen bond in the former. When present in intramolecularly ionized structures, which increase its stability in the excited state to a greater extent than in the ground state, this type of bond should produce a shift in band B toward longer wavelengths in comparison with its position for o-nitroacetophenone and in actual fact this is not the case. The reason for this difference in the absorption curves of o-nitrobenzaldehyde and o-nitroacetophenone should apparently be sought in forms of interaction of functional groups in an ortho-position, different from a hydrogen bond [9, 15].

SUMMARY

1. The results of measuring the absorption curves of o-, m- and p-nitrobenzaldehydes in 7 different solvents are presented.
2. The absorptions of nitrobenzaldehydes are determined by the same electron transitions as in unsubstituted nitrobenzene and nitroacetophenones.
3. The peculiarities in the light absorption of o-nitrobenzaldehyde in comparison with that of o-nitroacetophenone does not indicate that the former contains an intramolecular hydrogen bond involving the hydrogen of the aldehyde group.

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UNSATURATED HYDROCARBONS

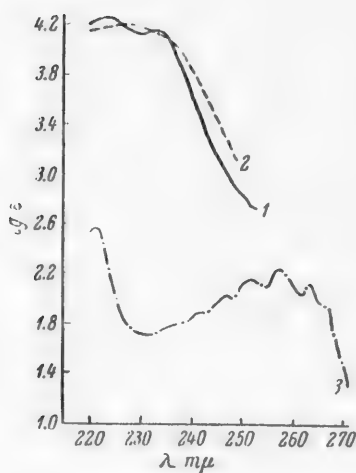
VIII. SYNTHESIS AND SOME CONVERSIONS OF 3-PHENYLHEPTADIEN-4,6-OL-3

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In previous work [1] it was shown that in the aromatization of aryl-substituted acetylenic, ethylenic and saturated γ -glycols and the tetrahydrofuran and saturated hydrocarbon, corresponding to them, diphenyl derivatives were obtained as the main reaction products.

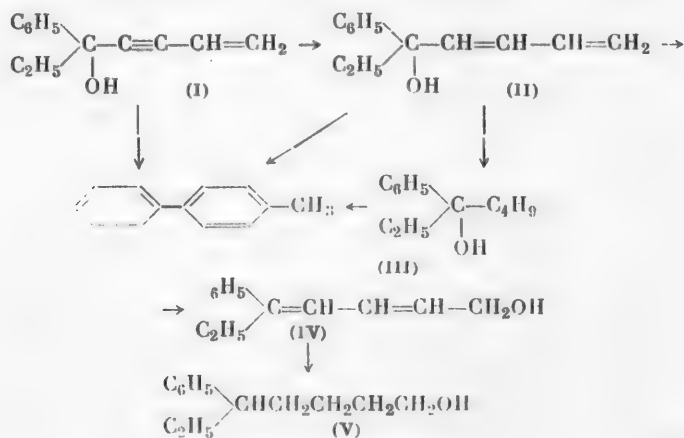
Since the synthesis and properties of acetylenic alcohols and glycols have been studied in our laboratory for a number of years, we undertook to determine whether the same conversions occur in the case of vinylacetylene alcohols and their derivatives. For this purpose we chose ethylphenylvinylethynylcarbinol (I), which was previously synthesized by one of us [2]. When reduced with lithium aluminum hydride, it gave a high yield of 3-phenylheptadien-4,6-ol-3 (II). When the latter was hydrogenated over Raney nickel catalyst, 2 moles of hydrogen were absorbed and the compound was smoothly converted into 3-phenylheptanol-3 (III). Aromatization of these alcohols led to p-methyldiphenyl with a product yield that was low in the case of the vinylacetylenic alcohol, but increased sharply on going to the diene and saturated alcohols.



UV absorption spectra (in 95% alcohol). 1) 3-Phenylhept-6-yn-4-ol-3 (I), 2) 3-phenylheptadien-4,6-ol-3 (II), 3) 3-phenylheptanol-3 (III).

It is also conceivable that these alcohols could be aromatized in another direction, in which the main product should be o-methyldiphenyl. However, when appropriate fractions of the catalyzate were oxidized, o-phenylbenzoic acid was not detected and only p-phenylbenzoic acid was isolated.

Under the action of a dioxane solution of sulfuric acid [3], 3-phenylheptadien-4,6-ol-3 was isomerized into 5-phenylheptadien-2,4-ol-1 (IV), which was hydrogenated on a Raney nickel catalyst with the absorption of 2 moles of hydrogen and formed propiophenone on ozonization.



EXPERIMENTAL

Ethylphenylcarbinol was obtained from benzaldehyde by a Grignard synthesis in 92.7% yield and had b. p. 88-90° (5 mm), n_D^{20} 1.5240 [4]. It was converted into propiophenone by oxidation with chromic mixture; the yield was 89.7% and the product had b. p. 78-79° (5 mm), n_D^{20} 1.5330 [5].

3-Phenylhepten-6-yn-4-ol-3 (I) was synthesized in 89.6% yield as described previously [2]; the product had b. p. 114-115° (4 mm), n_D^{20} 1.5505; it crystallized on cooling and had m. p. 32-33°. The UV absorption spectrum is shown in the figure.

Preparation of 3-phenylheptadien-4,6-ol-3 (II). With stirring, 93 g of carbinol (I) in ether was added over a period of 1 hour to 1 liter of an ether solution of lithium aluminum hydride, obtained from 99.75 g of aluminum chloride and 36 g of lithium hydride. The reaction mixture was boiled on a water bath for 5-6 hours, cooled,

Aromatization of Alcohols over 25 ml of the Catalyst $MgO (Cr_2O_3) Al_2O_3 (2:18:30)$

Expt. No.	Starting alcohol	Temperature	Amount of alcohol introduced (in g)	Input rate (kg/liter cat.·hour)	Yield of p-methyldiphenyl (in %)
1	3-Phenylhepten-6-yn-4-ol-3 (I)	480°	8.2	0.33	9.2
2	3-Phenylheptadien-4,6-ol-3 (II)	460	8.0	0.32	33.2
3		482	8.0	0.32	31.7
4		480	11.6	0.44	24.4
5		502	8.2	0.45	17.1
6		520	8.1	0.36	17.9
7	3-Phenylheptanol-3 (III)	500	8.2	0.46	16.6
8		528	7.8	0.45	17.1
9		550	8.4	0.46	14.4
10		570	7.9	0.46	26.5
11		530	8.0	0.35	26.3
12		530	8.1	0.21	25.5

decomposed with moist ether, water and 2-5% sulfuric acid and extracted. After removal of the ether, the product was vacuum distilled. We obtained 85.5 g (91%) of 3-phenylheptadien-4,6-ol-3 as a colorless, pleasant smelling liquid. The UV absorption spectrum is presented in the figure.

B. p. 105-106° (4 mm), d_4^{20} 0.9872, n_D^{20} 1.5495, MR_D 60.62; Calc. 59.22.

Found %: C 82.46; H 8.96. $C_{15}H_{16}O$. Calculated %: C 82.93; H 8.55.

Carbinol (I) could be reduced in dioxane. In this case the yield was 83%.

When 1.5 g of diene alcohol (II) was hydrogenated over Raney nickel in 7 ml of methanol, 420 ml of hydrogen was absorbed (2 moles per mole) and we isolated 1 g of 3-phenylheptanol-3 (III) with b. p. 108-109° (8 mm), n_D^{20} 1.5058 [2].

Isomerization of 3-phenylheptadien-4,6-ol-3. A solution of 48 g of diene alcohol in 720 ml of 70% aqueous dioxane, containing 1% sulfuric acid, was heated at 40-45° for 10 hours. The cooled reaction mixture was saturated with potassium carbonate, the dioxane layer separated and the aqueous layer extracted with ether. The solvent was distilled from the combined dioxane-ether solution and the residue distilled. About 17 g of the original alcohol was recovered. The yield of 5-phenylheptadien-2,4-ol-1 (IV) was 18 g (37.5%).

B. p. 134-134° (1.5 mm), d_4^{20} 1.0075, n_D^{20} 1.5920, MR_D 63.07; Calc. 59.22.

Found %: C 82.56; H 8.77. $C_{15}H_{16}O$. Calculated %: C 82.90; H 8.53.

Ozonization of 2.95 g of 5-phenylheptadien-2,4-ol-1 yielded 1.13 g of propiophenone, whose 2,4-dinitrophenylhydrazone did not depress the melting point of the authentic substance (mixed melting point 189-190° [5]).

When 2.08 g of the alcohol was hydrogenated in 8 ml of methanol on Raney nickel, 540 ml of hydrogen was absorbed (2 moles per mole) and we isolated 1.7 g of 5-phenylheptanol-1 (V).

B. p. 134-135° (3 mm), n_D^{20} 1.5085, d_4^{20} 0.9525, MR_D 60.13; Calc. 60.16.

Found %: C 80.67; H 10.41. $C_{15}H_{20}O$. Calculated %: C 81.19; H 10.48.

Aromatization was carried out on a $MgO(Cr_2O_3)Al_2O_3$ (2:18:80) catalyst as described previously [1]. The starting carbinol was introduced into the catalytic furnace as a 20% solution in benzene. The p-methyldiphenyl obtained had m. p. 46-47° (from CH_3OH) [1] and a mixture with an authentic sample melted at 47-47.5°. Oxidation of appropriate fractions of the catalyzate with 2% potassium permanganate yielded p-phenylbenzoic acid with m. p. 123-124° (from 60% ethanol) and a mixed melting point with authentic acid was not depressed. The results of some of the experiments are presented in the table.

The authors are very grateful to Z. P. Trotsenko for carrying out the analyses.

SUMMARY

1. Aromatization over an aluminochromium catalyst of ethylphenylvinylethynylcarbinol and the products of its partial and complete hydrogenation led to p-methyldiphenyl.

2. Under the action of sulfuric acid, 3-phenylheptadien-4,6-ol-3 isomerized into 5-phenylheptadien-2,4-ol-1.

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UNSATURATED HYDROCARBONS

IX. CONTRIBUTION ON THE AROMATIZATION OF ARYL SUBSTITUTED COMPOUNDS

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We previously showed [1] that the aromatization of aryl substituted glycols, namely 2-methyl-5-phenyl-hexyne-3-diol-2,5 (I) and the products of its partial and complete (II) hydrogenation, led to the formation of p-methyldiphenyl (III). In the aliphatic series, substituted tetrahydrofurans give on aromatization the same products as the glycols and hydrocarbons corresponding to them [2, 3]. Aromatization of aryltetrahydrofurans has not been described in the literature.

In connection with this we achieved the conversion of 2,2,5-trimethyl-5-phenyltetrahydrofuran (IV) over the catalyst $\text{MgO}(\text{Cr}_2\text{O}_3) \text{ Al}_2\text{O}_3$ (2 : 18 : 80) and showed that the main product in this case was p-methyldiphenyl.

In examples of aromatization of aliphatic-aromatic hydrocarbons known up to the present, compounds with condensed nuclei were obtained as a rule [4-7].

So as to establish whether the reaction direction found was of general value and to elucidate the role of potential unsaturation in the formation of molecules of the diphenyl type, we aromatized 2-methyl-5-phenyl-hexane (V), which was also found to give p-methyldiphenyl. We were unable to detect condensed systems in the reaction products. The molecule of the original hydrocarbon had a methyl group in position 2, which could have hindered cyclization into the corresponding naphthalene. We therefore aromatized 2-(4'-methylphenyl)-hexane (VI) and again obtained only p-methyldiphenyl.

The conversions were carried out according to the scheme:

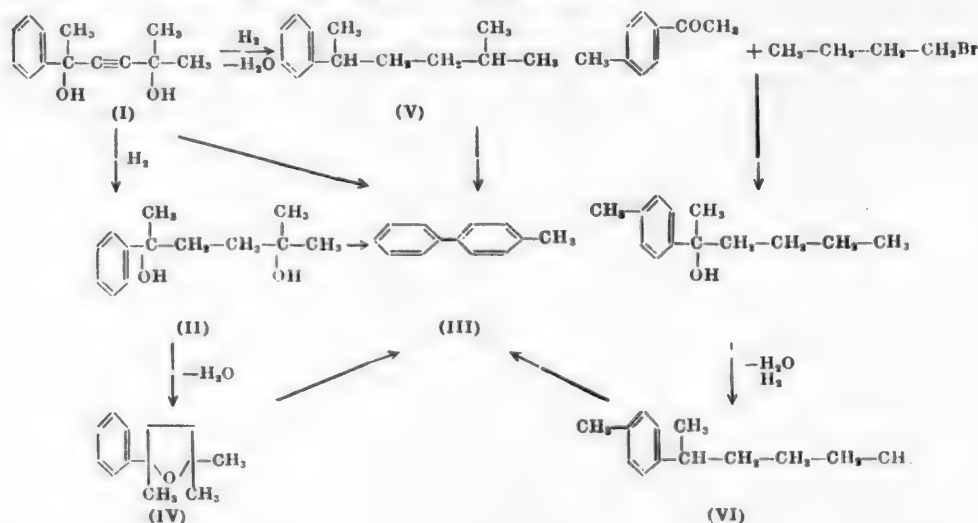


TABLE 1

Aromatization of 2,2,5-Trimethyl-5-phenyltetrahydrofuran over the Catalyst $\text{MgO}(\text{Cr}_2\text{O}_3)\text{Al}_2\text{O}_3$ (2:18:80)

Expt. No.	Temperature	Amount of tetrahydrofuran introduced* (in g)	Input rate (kg/liter cat./hour)	p-Methyldiphenyl yield	
				(in g)	(in %)
1	497°	6.7	0.36	1.5	25.4
2	530	6.8	0.36	1.8	30.0
3	550	8.5	0.36	2.6	34.6
4	550	7.2	0.16	1.3	20.6
5	555	7.6	0.57	1.8	26.7
6	570	7.4	0.37	1.1	16.8
7	550	7.3	0.26	2.75	42.5
8	550	8.0	0.36	3.34**	47.2
9	550	8.3	0.40	3.32	45.5

* In Experiments 1-6, the tetrahydrofuran was introduced without dilution and in Experiments 7-9, as a 20% solution in benzene.

** About 75% of the total catalyzate (without benzene).

TABLE 2

Aromatization of 2-(4'-methylphenyl)-hexane over the Catalyst $\text{MgO}(\text{Cr}_2\text{O}_3)\text{Al}_2\text{O}_3$ (2:18:80)

Expt. No.	Temperature	Amount of hexane introduced (in g)	Input rate (kg/liter cat./hour)	p-Methyldiphenyl yield *	
				(in g)	(in %)
12	550°	8.0	0.20	2.17	28.4
13	552	8.4	0.35	1.68	20.9
14	575	7.6	0.21	1.63	22.4
15	572	8.1	0.36	2.45	31.5
16	578	8.0	0.58	2.32	30.4

* None of the catalyzate fractions formed a picrate.

EXPERIMENTAL

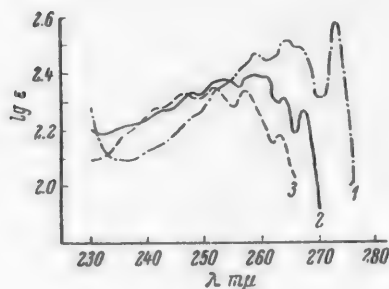
2,2,5-Trimethyl-5-phenyltetrahydrofuran. Dry hydrogen chloride was passed for 1 hour into a solution of 91 g (0.437 mole) of 2-methyl-5-phenylhexanediol-2,5 in 500 ml of benzene at room temperature. About 8 ml of water was thus liberated. The reaction mass was neutralized with sodium bicarbonate solution, washed with water and dried with calcium chloride. Removal of the benzene and vacuum distillation of the residue yielded 71.5 g (86%) of 2,2,5-trimethyl-5-phenyltetrahydrofuran with b. p. 80.5-81° (2.5 mm), n_D^{20} 1.5000; literature data [8]: b. p. 71° (0.4 mm), n_D^{20} 1.5002. The ultraviolet absorption spectrum, plotted on an SF-4 spectrophotometer, is shown in the figure.

Aromatization of 2,2,5-trimethyl-5-phenyltetrahydrofuran into p-methyldiphenyl was carried out over 25 ml of the catalyst $\text{MgO}(\text{Cr}_2\text{O}_3)\text{Al}_2\text{O}_3$ (2:18:80) in the flow apparatus described previously [1]. After distillation from a Claisen flask, the fraction with b. p. 150-180° (45 mm) contained (as was established by distillation on a column) about 80% of p-methyldiphenyl with b. p. 140-141° (16 mm) and m. p. 47-47.5° (from methanol), undepressed by admixture with an authentic sample.

When benzene was used as a diluent, the yield of the desired product was increased by 10-15%.

The results of the experiments are presented in Table 1.

2-Methyl-5-phenylhexane was obtained by heating 99 g (0.486 mole) of 2-methyl-5-phenylbutyn-3-diol-2,5, and 2 g of p-toluenesulfonic acid at 65-80° (5-30 mm) in a stream of nitrogen. After removal of the water the mass was cooled, dissolved in ether and washed with sodium bicarbonate solution and water. The ether was distilled from the calcium chloride dried solution and the residue dissolved in methanol. After removal of the precipitated polymer, the product was hydrogenated over Raney nickel at room temperature with an initial pressure of 50-60 atm, vacuum distilled [b. p. 85-110° (3.5 mm), n_D^{20} 1.5000-1.5140] and again dehydrated by heating under reduced pressure (140-160 mm) with 20 g of baked potassium bisulfate, 27 g of olefins [b. p. 92-94° (5 mm), n_D^{20} 1.5128] in methanol was hydrogenated over Raney nickel at room temperature and an initial pressure of 90 atm until the absorption of hydrogen ceased. The yield of 2-methyl-5-phenylhexane was 21.4 g (25%).



Ultraviolet absorption spectra in 95% alcohol. 1) 2-(4'-Methylphenyl)-hexane, 2) 2-methyl-5-phenylhexane, 3) 2,2,5-trimethyl-5-phenyltetrahydrofuran.

B. p. 222-224°, 65.5-66° (1.5 mm); 76-77° (3 mm), n_D^{20} 1.4886, d_4^{20} 0.8662, MR_D 58.61; Calc. 58.63.

Literature data [9]: b. p. 223°, d_4^{15} 0.8696.

The ultraviolet absorption spectrum is given in the figure.

Aromatization of 2-methyl-5-phenylhexane was similar to the aromatization of 2,2,5-trimethyl-5-phenyltetrahydrofuran described above. At 550°, an input rate of 0.24 kg/liter cat./hour and without diluent, 6.1 g of 2-methyl-5-phenylhexane yielded 1.15 g (19.8%) of p-methyldiphenyl. At 570° and an input rate of 0.44 kg/liter cat./hour (20% solution in benzene) the yield of p-methyldiphenyl was only 16.9%; the product had m. p. 46.5-47.5° (from methanol), undepressed by admixture with an authentic sample.

None of the catalyze fractions gave a picrate under normal conditions.

2-(4'-Methylphenyl)-hexanol-2 was obtained by adding 77.5 g (0.578 mole) of 4-methylacetophenone [b. p. 102-103° (14 mm)] to a cooled ether solution of butylmagnesium bromide, prepared from 14.1 g (0.588 mole) of magnesium and 82.3 g (0.06 mole) of butyl bromide, and stirring the mixture for several hours at room temperature. The mass was decomposed with water and 5-10% sulfuric acid. The ether layer was washed with sodium bicarbonate solution and water and dried with potassium carbonate. Removal of the solvent yielded 93.2 g (85.5%) of 2-(4'-methylphenyl)-hexanol-2.

B. p. 106-107° (2 mm), n_D^{20} 1.5084, d_4^{20} 0.9478, MR_D 60.45; Calc. 60.16.

Found %: C 80.95, 81.00; H 10.37, 10.42. $C_{13}H_{20}O$. Calculated %: C 81.18; H 10.48.

Dehydration of 2-(4'-methylphenyl)-hexanol-2. 50 g (0.26 mole) of carbinol was heated with 30 g of baked potassium bisulfate under reduced pressure (100-150 mm), the liberated water removed by distillation and the residue distilled. The yield of olefins was 41.5 g (91.5%) and the product had b. p. 84-87° (2 mm), n_D^{20} 1.5243.

2-(4'-Methylphenyl)-hexane. 49.5 g (0.284 mole) of dehydration product in 75 ml of methanol was hydrogenated over Raney nickel at room temperature and an initial hydrogen pressure of 90 atm until the absorption of hydrogen ceased. After removal of the solvent, the residue was vacuum distilled.

B. p. 84-85° (4 mm), n_D^{20} 1.4908.

Literature data [10]: b. p. 162-165° (135 mm), n_D^{20} 1.4910.

The ultraviolet absorption spectrum is presented in the figure.

Aromatization of 2-(4'-methylphenyl)-hexane was under the same conditions as for 2,2,5-trimethyl-5-phenyltetrahydrofuran. The results of some experiments are presented in Table 2.

The p-methyldiphenyl obtained had m. p. 47-47.5° (from methanol).

SUMMARY

Aromatization of alkylbenzenes containing not less than six carbon atoms in the side chain leads to the formation of diphenyls.

2,2,5-Trimethyl-5-phenyltetrahydrofuran was aromatized into p-methyldiphenyl.

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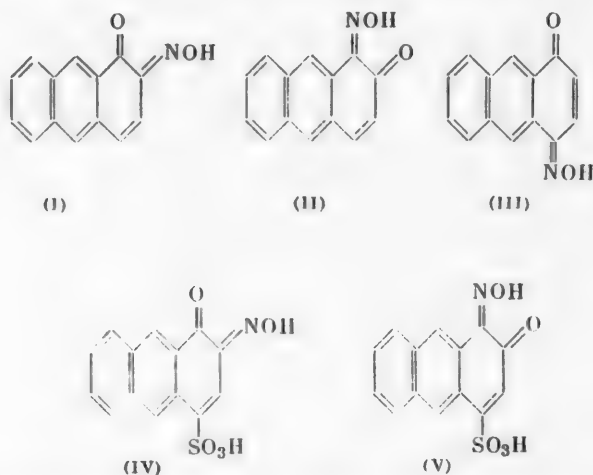
INVESTIGATION IN THE FIELD OF HYDROXY DERIVATIVES OF ANTHRACENE

VI. REACTIVITY OF NITROSOANTHROLS AND NITROSOANTHROLSULFONIC ACIDS

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In contrast to 1-nitroso-2-anthrol (II) and 4-nitroso-1-anthrol (III) [1, 2], 2-nitroso-1-anthrol (I) does not add bisulfite, while 2-nitroso-1-anthrol-4-sulfonic acid (IV), in contrast to 1-nitroso-2-anthrol-4-sulfonic acid (V), does not exchange the sulfonyl group either in aqueous solutions of alkalis or in solutions of aromatic amines [3].



An investigation showed that this difference could not be explained by a benzoid structure for 2-nitroso-1-anthrol and 2-nitroso-1-anthrol-4-sulfonic acid. All three nitrosoanthrols are capable of reacting in the quin-oxime form: for example, they form the corresponding dioximes with hydroxylamine. As the β -carbon atoms have the lowest electron density in the anthracene ring [4], the carbonyl group in (II) will be more active with regard to the nucleophilic hydroxylamine than those in (I) and (III). While heating with hydroxylamine for 1 hour was sufficient to convert 1-nitroso-2-anthrol (II) into 1,2-anthraquinonedioxime, 2-nitroso-1-anthrol (I) was not more than 70% changed even after 20 hours. The difference in the activity of the α - and β -carbonyl groups is clearly shown by the example of 1,2-anthraquinone, which forms exclusively the 2-oxime when boiled with hydroxylamine hydrochloride. The monoximes obtained from 1,2- and 1,4-anthraquinones were identical to 2-nitroso-1-anthrol (I) and 4-nitroso-1-anthrol (III) respectively.

Methylation of the silver salts of 2-nitroso-1-anthrol (I) [5] and 1-nitroso-2-anthrol (II) [6] and the sodium salt of 4-nitroso-1-anthrol (III) led to ethers of the quinoneoximes. In the cases of (I) and (II), this was established by conversion of the ethers into 1,2-anthra-(3, 4')-furazan by successive treatment with hydroxylamine and sodium hydroxide solution, and in the case of (III), by the formation of the dimethyl ether of 1,4-anthraquinone-dioxime when the ether of (III) was condensed with O-methylhydroxylamine hydrochloride. For comparison, the

dimethyl ether of 1,4-anthraquinonedioxime was prepared from 1,4-anthraquinone and O-methylhydroxylamine or from 1,4-anthraquinonedioxime. The dimethyl ether of 1,2-anthraquinonedioxime was obtained by the action of O-methylhydroxylamine on the methyl ether of 1-nitroso-2-anthrol. Methylation of silver salt of 4-nitroso-1-anthrol (III) led to a compound with the same composition and the same melting point as that from methylation of the sodium salt; however, the absorption spectra of the substances (Fig. 3) were not identical and a mixture of the substances melted with a depression of 16°. The structure of the product from methylation of the silver salt of 4-nitroso-1-anthrol was not investigated.

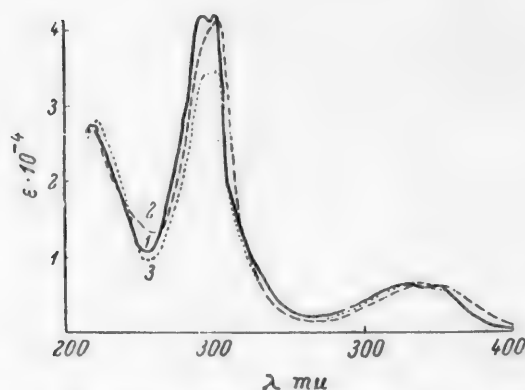


Fig. 1. Absorption spectra in alcohol. 1) 2-Nitroso-1-anthrol (I), 2) methyl ether of 2-nitroso-1-anthrol, 3) 2-nitroso-1-anthrol-4-sulfonic acid (V).

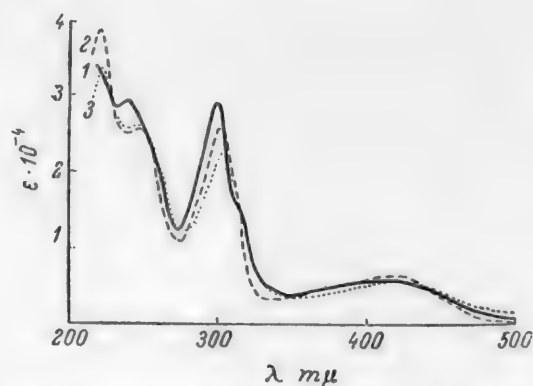
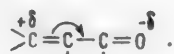


Fig. 2. Absorption spectra in alcohol. 1) 1-Nitroso-2-anthrol (II), 2) methyl ether of 2-nitroso-1-anthrol, 3) 1-nitroso-2-anthrol-4-sulfonic acid (V).

As a comparison of the absorption spectra of the nitrosoanthrols and their methyl ethers (Figs. 1-3) shows, methylation of 2-nitroso-1-anthrol (I) and 1-nitroso-2-anthrol (II) is accompanied by a bathochromic, and methylation of 4-nitroso-1-anthrol (III) by a hypsochromic shift in the absorption curve. The same change in the absorption spectra was observed on methylation of nitrosonaphthols [7]. It is known that in the series nitrosophenol → ether of nitrosophenol → ether of benzoquinoneoxime → benzoquinoneoxime there is a shift in the spectra toward shorter wavelengths [8]. By applying this rule to nitrosonaphthols, Baltazzi arrived at the conclusion that at least in alcohol solutions, 1-nitroso-2-naphthol and 2-nitroso-1-naphthol were predominantly in the quinoxime and 4-nitroso-1-naphthol was predominantly in the nitrosophenol form [7].

The absorption spectra of 2-nitroso-1-anthrol-4-sulfonic acid (IV) and 1-nitroso-2-anthrol-4-sulfonic acid (V) were close to the spectra of the corresponding nitrosoanthrols (Figs. 1 and 2). As in the case of other quinoid compounds [9], the introduction of sulfonic groups produces a very slight shift into the longwave region. In addition to the character of the electronic spectra, the possibility of preparing (IV) from 1,2-anthraquinone- or 1,2-anthraquinonedioxime-4-sulfonic acids [3] and the exceptionally great lability of the sulfonic group in 1,2-anthraquinone-4-sulfonic acid and (V) indicate that the nitrosoanthrolsulfonic acids (IV) and (V) probably have a quinoxime structure.

The addition of bisulfite to the quinoxime form of nitrosoanthrols (II) and (III), which occurs as in the case of α,β -unsaturated ketones [10], at the carbon double bond, should evidently be considered as 1,4-addition of nucleophilic reagents to a conjugated system:



The addition of arylamino or hydroxy groups to 1-nitroso-2-anthrol-4-sulfonic acid (V), which is accompanied by subsequent elimination of a bisulfite ion, has the same character. In contrast to (II), (III), and (V), (I) and

(IV) have the double bond in the quinoid nucleus in conjugation not with the carbonyl, but with the oxime group, which naturally has considerably lower electron-acceptor properties. Due to the insignificant polarization of the bonds in the system $\text{>C}=\text{C}-\text{C}=\text{N}-\text{OH}$ 1,4-addition of nucleophilic reagents to (I) and (IV) must require a high activation energy and be impossible under mild conditions.

As the properties of nitrosoanthrols and nitrosoanthrolsulfonic acids are analogous to the properties of the corresponding naphthalene derivatives [11], the ideas presented are quite applicable to compounds of the naphthalene series.

EXPERIMENTAL

2-Nitroso-1-anthrol (I). A mixture of 1.04 g of 1,2-anthraquinone prepared by oxidation of potassium 2-anthrolnitrosodisulfonate [12], 0.36 g of hydroxylamine hydrochloride and 100 ml of 90% alcohol was boiled for 1 hour and then the bulk of the alcohol was removed and water added. The precipitate was collected, washed well and boiled in a dilute solution of sodium hydroxide. The insoluble part (0.37 g) consisted of colorless plates with m. p. 178-180° (from alcohol); a mixture with 1,2-anthrafurazan had m. p. 156°; the substance was not investigated. Acidification of the alkaline solution yielded 0.56 g (52%) of nitrosoanthrol. A mixture of the methyl ether, which had m. p. 134°, with the methyl ether of 2-nitroso-1-anthrol, obtained from 1-anthrol [5], had m. p. 134°.

Behavior toward bisulfite. 0.4 g of 2-nitroso-1-anthrol (I) was heated with a mixture of 10 ml of water, 2 g of 38% sodium bisulfite and a drop of pyridine at 50° for 8 hours. Filtration of the suspension gave a quantitative yield of unchanged nitrosoanthrol and no traces of bisulfite compound were detected in the colorless filtrate.

Interaction with hydroxylamine. A solution of 0.5 g of (I), 0.5 g of hydroxylamine hydrochloride and 1 g of crystalline sodium acetate in 50 ml of 90% alcohol was boiled for 20 hours. After removal of the alcohol and addition of water, the precipitate was collected and heated at 90° for 30 minutes in dilute sodium hydroxide. The alkali-insoluble 1,2-anthrafurazan was collected and acidification of the filtrate yielded unreacted nitrosoanthrol. We isolated 0.33 g (64%) of 1,2-anthrafurazan and 0.145 g (29%) of (I). Under analogous conditions, but with the alcohol solution boiled for 1 hour, from (I) we obtained only 0.47 g (94%) of unchanged substance and from (II), 0.45 g (91%) of 1,2-anthrafurazan.

The methyl ether of 2-nitroso-1-anthrol was converted into 1,2-anthrafurazan under the same conditions as for (I). After the former had been boiled with hydroxylamine, heated in 10% sodium hydroxide and sublimed in vacuum, we isolated a substance with m. p. 172-173°, a mixture of which with 1,2-anthrafurazan melted at 173.5-174°. The methyl ether of 1-nitroso-2-anthrol [6] yielded 1,2-anthrafurazan with m. p. 175-175.5°.

4-Nitroso-1-anthrol (III). 1.04 g of 1,4-anthraquinone, obtained by oxidation of potassium 1-anthrolnitrososulfonate

[13], was treated with hydroxylamine hydrochloride similarly to 1,2-anthraquinone. The residue isolated by removal of the alcohol was dissolved in dilute sodium hydroxide at room temperature. The solution was filtered to remove tarry impurities and acidified. For purification, the precipitated nitrosoanthrol was converted into the bisulfite compound [1], which was decomposed to give a yield of 0.4 g (37%) of (III).

Interaction with hydroxylamine. 0.5 g of 4-nitroso-1-anthrol (III) was treated with hydroxylamine as described for (II). After partial removal of the alcohol, clarification of the solution with charcoal and cooling, 0.35 g of light yellow needles was obtained. The acetyl derivative had m. p. 232° (decomp.) and a mixture of it with the diacetyl derivative of 1,4-anthraquinonedioxime [1] had m. p. 233° (decomp.).

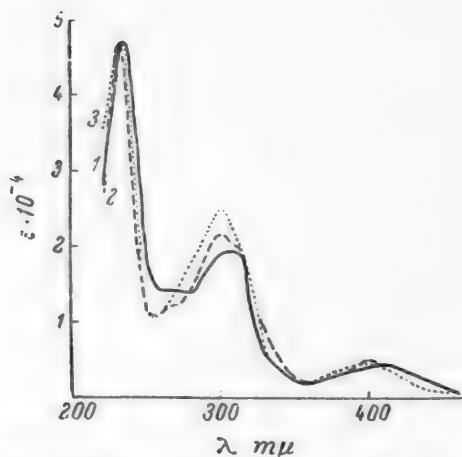


Fig. 3. Absorption spectra in alcohol. 1) 4-Nitroso-1-anthrol (III), 2) methyl ether of 4-nitroso-1-anthrol (from Na salt), 3) methyl ether of 4-nitroso-1-anthrol (from Ag salt).

Methyl ether. a) To a solution of 0.4 g of (III) in dilute sodium hydroxide was added 2 ml of dimethyl sulfate and the mixture shaken vigorously. After a few minutes a precipitate began to form and this was collected, washed until neutral and recrystallized from aqueous alcohol. The yield was 0.204 g. The light yellow needles (from alcohol) had m. p. 135°.

Found %: N 6.04. $C_{15}H_{11}O_3N$. Calculated %: N 5.90.

b) A solution of 0.38 g of (III) in 17 ml of 0.1 N alcoholic potassium hydroxide was evaporated and to an aqueous solution of the potassium salt formed was added a solution of 0.4 g of silver nitrate. The gelatinous, red precipitate of the silver salt of (III) was collected, washed with water, dried in vacuum and powdered. A mixture of the silver salt, 20 ml of alcohol, 20 ml of ether and 1 ml of methyl iodide was boiled for 3 hours and filtered. The filtrate was partially evaporated, clarified with charcoal and diluted with water. The precipitated substance was recrystallized many times from alcohol. The light yellow needles were insoluble in water and alkalis and readily soluble in organic solvents and had m. p. 134.5°-135.5°; a mixture with the substance obtained in case "a" had m. p. 118°.

Found %: C 75.76; H 4.88; N 5.92. $C_{15}H_{11}O_3N$. Calculated %: C 75.93; H 4.67; N 5.90.

Dimethyl ether of 1,4-anthraquinonedioxime. a) A mixture of 1 g of 1,4-anthraquinone, 1 g of O-methylhydroxylamine hydrochloride and 50 ml of alcohol was boiled for 1 hour and the solution clarified with charcoal and filtered. On cooling, the solution deposited long, light yellow needles. The yield was 0.51 g and the m. p. 160.5-160.8°.

b) A solution of 0.1 g of the methyl ether of (III), obtained by variant "a", and 0.1 g of O-methylhydroxylamine hydrochloride in 10 ml of alcohol was boiled for 3 hours and partially evaporated. On cooling, the solution deposited long needles with m. p. 160.5-161° (from alcohol); a mixture with the dimethyl ether prepared from 1,4-anthraquinone (variant "a") had m. p. 160.5-161°.

c) A solution of 1,4-anthraquinonedioxime in dilute sodium hydroxide was shaken with dimethyl sulfate. The precipitate was collected and recrystallized from alcohol 160.5-161°.

Found %: C 72.07; H 5.20; N 10.51. $C_{16}H_{14}O_2N_2$. Calculated %: C 72.16; H 5.30; N 10.52.

Dimethyl ether of 1,2-anthraquinonedioxime. A solution of 0.4 g of the methyl ether of (II), 0.4 g of crystalline sodium acetate and 0.25 g of O-methylhydroxylamine hydrochloride in 20 ml of 90% alcohol was boiled for 2 hours and partially evaporated. On cooling, the solution deposited clusters of pale yellow needles (0.31 g); after recrystallization from alcohol, the substance had m. p. 104.5-105°.

Found %: N 10.54. $C_{16}H_{14}O_2N_2$. Calculated %: N 10.52.

Spectroscopy. Solutions of the substances in alcohol at concentrations of 10^{-4} and $0.2 \cdot 10^{-4}$ μ were used for spectroscopy. The measurements were made on an SF-4 spectrophotometer at 5 m μ intervals with the positions of the maxima determined more accurately.

SUMMARY

1. By the action of hydroxylamine, nitrosoanthrols-1,2, -2,1 and -1,4 were converted into the corresponding anthraquinonedioximes and by methylation, into ethers of the corresponding anthraquinonemonooximes. The monooximes obtained from 1,2- and 1,4-anthraquinone were identical to 2-nitroso-1-anthrol and 4-nitroso-1-anthrol, respectively.

2. The incapacity of 1,2-anthraquinone-2-oxime to add bisulfite and the low lability of the sulfonic group in 1,2-anthraquinone-2-oxime-4-sulfonic acid may be explained by the weak electron-acceptor properties of the oxime group, hindering 1,4-addition of nucleophilic reagents.

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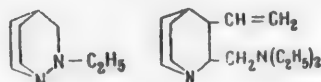
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THERMAL DECOMPOSITION OF ESTERS OF N-SUBSTITUTED
7-AMINOMETHYL-6-(β -HYDROXYETHYL)-1-AZABICYCLO-(3,2,1)-OCTANE

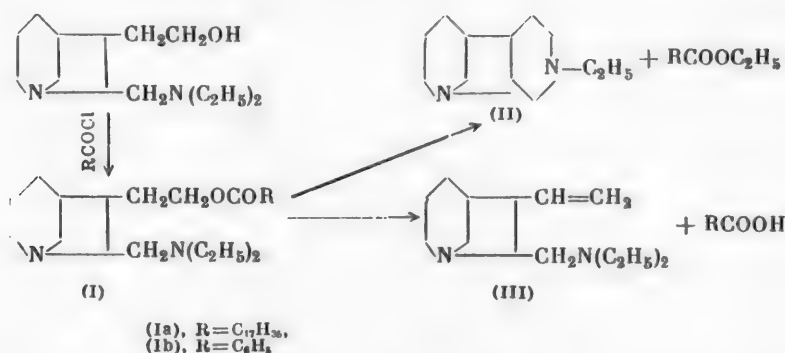
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In a previous communication [1] we showed that distillation of the benzoic and stearic esters of 2-diethylaminomethyl-3-(β -hydroxyethyl)-quinuclidine at atmospheric pressure formed mainly 2,3-(3',4'-N-ethylpiperidino)-quinuclidine and in the case of the stearic ester, together with the tricyclic compound, a small amount (not more than 10% of the total substances) of 2-diethylaminomethyl-3-vinylquinuclidine was obtained.



In the present work we studied the high temperature cleavage of the benzoic and stearic esters of 7-diethylaminomethyl-6-(β -hydroxyethyl)-1-azabicyclo-(3,2,1)-octane. The bicyclic system, 1-azabicyclo-(3,2,1)-octane, is isomeric with quinuclidine [1-azabicyclo-(2,2,2)-octane] and consequently one would expect analogies in the behavior of corresponding derivatives during distillation. Actually, it was found that distillation of the benzoic and stearic esters of 7-diethylaminomethyl-6-(β -hydroxyethyl)-1-azabicyclo-(3,2,1)-octane (Ia and Ib) at atmospheric pressure also formed a tricyclic system, which in this case had the structure of 6,7-(3',4'-N-ethylpiperidino)-1-azabicyclo-(3,2,1)-octane (II). There was the simultaneous formation of a considerable amount of 7-diethylaminomethyl-6-vinyl-1-azabicyclo-(3,2,1)-octane (III), which was not observed in distillation of analogous esters of quinuclidine.

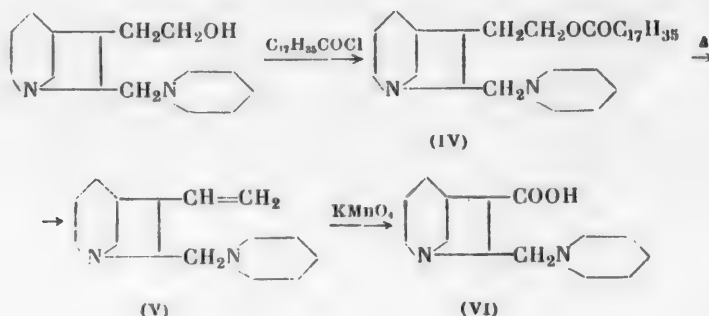


Apart from the two substances indicated, (II) and (III), the distillation products contained (depending on the ester distilled) stearic acid and its ethyl ester or benzoic acid and its ethyl ester, respectively. The presence of stearic or benzoic acid in the reaction mixture after distillation of the esters (I) was caused by the formation of the vinyl compound (III) during this process and the formation of the ethyl esters of stearic and benzoic acids was explained by the parallel conversion of esters (I) into the tricyclic compound (II).

Compounds (II) and (III) were separated by treatment of the mixture of substances with mercury acetate with subsequent separation of the addition products of mercury acetate and the unsaturated compound and decomposition of the latter with phosphorous acid.

We then studied the cleavage of 7-(N-piperidinomethyl)-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane (IV) during distillation at atmospheric pressure. In this compound, in contrast to esters (I), the side chain in position 7 contained nitrogen, forming part of a cyclic system, which could not be cleaved at high temperature and participate in the formation of a stearic ester molecule. Due to this, distillation of compound (IV) could only form 7-(N-piperidinomethyl)-6-vinyl-1-azabicyclo-(3,2,1)-octane (V) and this was confirmed by experiment.

By oxidation of compound (V) we obtained 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-7-carboxylic acid (VI) and its ethyl ester and hydrazide. The formation of acid (VI) by oxidation of the unsaturated compound (V) indicated that compound (V) contained a vinyl group in position 6.



EXPERIMENTAL

7-Diethylaminomethyl-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane (Ia). To a solution of 3.15 g of 7-diethylaminomethyl-6-(β -hydroxyethyl)-1-azabicyclo-(3,2,1)-octane [2] in 30 ml of benzene was added 4.4 g of stearoyl chloride with stirring. The reaction mixture was boiled for 3 hours, the solvent evaporated and the residue treated with 25% potassium carbonate solution and extracted with ether. The ether extract was dried with potassium carbonate and the solvent removed to give 6.55 g of 7-diethylaminomethyl-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane as a colorless, oily mass, which partially decomposed when vacuum distilled.

The iodomethylate formed colorless crystals which were soluble in alcohol and water, but insoluble in ether. The m. p. was 83-87° (from ether).

Found %: I 20.13. $C_{33}H_{55}O_2N_2I$. Calculated %: I 19.70.

Decomposition of 7-diethylaminomethyl-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane. 3.45 g of 7-diethylaminomethyl-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane was heated in a Wurtz flask on a metal bath at 300-350°. (The ester was decomposed in small portions since prolonged heating of large amounts of ester at high temperature was accompanied by considerable tar formation.) The soapy mass which distilled (2.62 g) was dissolved in ether and the ether solution extracted with 10% hydrochloric acid to remove basic substances and then evaporated. This yielded a mixture of stearic acid (0.45 g) with m. p. 70°* and 0.4 g of ethyl stearate with m. p. 33°*.* The hydrochloric acid extract was made alkaline with 50% potassium carbonate solution and extracted with ether. The ether extract was dried with potassium carbonate, the ether removed and the residue vacuum distilled. We obtained 0.5 g of a mobile, colorless oil, which gave a positive reaction for a double bond. The b. p. was 86° (0.1 mm). For separation of the unsaturated compound from the saturated substances, 3.6 g of mixture obtained from several experiments was dissolved in 31.8 g of 10% sulfuric acid and the sulfuric acid solution added to 75 g of a 10% solution of mercury acetate in 5% acetic acid solution. The reaction

* According to literature data [3]: m. p. 70.5-71°.

. According to literature data [3]: m. p. 34.7-35°.

mixture was heated for 8 hours at 40-50°, cooled to 0-5°, saturated with ammonia and extracted with ether. The ether solution was dried with potassium carbonate, the solvent removed and the residue vacuum distilled. We obtained 1.2 g of 6,7-(3',4'-N-ethylpiperidino)-1-azabicyclo-(3,2,1)-octane as a colorless, mobile liquid, which was soluble in water and organic solvents. The b. p. was 97° (0.33 mm) and n_D^{21} 1.5043.

Found %: C 73.88; H 11.32; N 14.57. $C_{12}H_{22}N_2$. Calculated %: C 74.24; H 11.34; N 14.42.

The picrate formed yellow crystals which were soluble in water, acetone and alcohol and insoluble in ether. The m. p. was 171° (decomp.).

Found %: C 44.65; H 4.38. $C_{12}H_{22}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 44.3; H 4.3.

After separation of 6,7-(3',4'-N-ethylpiperidino)-1-azabicyclo-(3,2,1)-octane, the ammonia solution contained the mercury complex of 7-diethylaminomethyl-6-vinyl-1-azabicyclo-(3,2,1)-octane. For decomposition of the mercury complex, the ammonia mother solution was acidified to Congo with 10% sulfuric acid, 2.74 g of phosphorous acid added and the mixture boiled for 7 minutes. The mercury liberated was removed by filtration, the filtrate treated with 50% potassium carbonate solution and extracted with ether. The ether extracts were dried with potassium carbonate, the ether removed and the residue distilled. We obtained 0.9 g of 7-diethylaminomethyl-6-vinyl-1-azabicyclo-(3,2,1)-octane as a colorless mobile liquid which was soluble in water and organic solvents. The b. p. was 83-84° (0.3 mm) and n_D^{17} 1.492.

Found %: C 75.45; 75.58; H 11.68, 11.62; N 12.92. $C_{14}H_{26}N_2$. Calculated %: C 75.65; H 11.73; N 12.62.

The picrate formed yellow crystals which were soluble in water and acetone and insoluble in ether. The m. p. was 82°.

Found %: C 45.25; H 4.25; N 16.22, 16.07. $C_{14}H_{26}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: C 45.3; H 4.7; N 16.5.

Decomposition of 7-diethylaminomethyl-6-(β -benzoyloxyethyl)-1-azabicyclo-(3,2,1)-octane. 1.4 g of 7-diethylaminomethyl-6-(β -benzoyloxyethyl)-1-azabicyclo-(3,2,1)-octane [2] was heated in a Wurtz flask on a metal bath at 340°. We collected 0.8 g of distillate with b. p. 260-265°. The distillate was dissolved in 10% hydrochloric acid and the solution extracted with ether to separate the basic substances. The ether extract was evaporated to give a mixture of benzoic acid and ethyl benzoate. To separate these, the mixture was dissolved in 10 ml of water and the benzoic acid titrated with 0.1 N sodium hydroxide solution. We obtained 0.195 g of benzoic acid (by titration). The m. p. was 119°.* The alkaline solution after the titration was extracted with ether. The ether extract was dried with potassium carbonate, the ether evaporated and the residue distilled. We obtained 0.18 g of ethyl benzoate with b. p. 212°.** The hydrochloric acid solution after separation of the benzoic acid and its ester was made alkaline with 50% potassium carbonate solution and extracted with ether. After drying the ether solution with potassium carbonate and removing the solvent, we distilled the residue. We obtained 0.4 g of a colorless, mobile oil with b. p. 85-90° (0.6 mm), giving a positive reaction for a double bond, and containing the tricyclic compound, 6,7-(3',4'-N-ethylpiperidino)-1-azabicyclo-(3,2,1)-octane, together with 7-diethylaminomethyl-6-vinyl-1-azabicyclo-(3,2,1)-octane. These substances were separated by the method described in the previous experiment.

From 0.7 g of mixture we isolated 0.4 g of 6,7-(3',4'-N-ethylpiperidino)-1-azabicyclo-(3,2,1)-octane with b. p. 97° (0.3 mm), n_D^{21} 1.5043 [picrate, m. p. 171° (decomp.)] and 0.3 g of 7-diethylaminomethyl-6-vinyl-1-azabicyclo-(3,2,1)-octane with b. p. 83-84° (0.3 mm), n_D^{17} 1.492 [picrate, m. p. 82°].

Preparation of 7-(N-piperidinomethyl)-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane and its decomposition. A solution of 13.36 g of 7-(N-piperidinomethyl)-6-(β -hydroxyethyl)-1-azabicyclo-(3,2,1)-octane [2] and 22 g of stearoyl chloride in 150 ml of anhydrous benzene was boiled for 4 hours. The benzene was removed in vacuum, the residue treated with 25 % potassium carbonate solution and the liberated oil extracted with ether. The ether extract was dried with sodium sulfate. Removal of the ether in vacuum yielded 38 g of 7-(N-piperidinomethyl)-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane as a soapy, uncrystallizable mass, which was soluble in organic solvents, but insoluble in water. 38 g of 7-(N-piperidinomethyl)-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane (in 5 g portions) was heated on a metal bath at 300°. The distillation products obtained from all the decomposition experiments were dissolved in ether. The ether solution was extracted with 10% hydrochloric

*According to literature data [3]: m. p. 120°.

**According to literature data [3]: b. p. 212.9°.

acid solution to separate the stearic acid from basic substances. The hydrochloric acid solution was made alkaline with 50% potassium carbonate solution and extracted with ether. When the ether solution had been dried with potassium carbonate and the solvent removed, the residue was vacuum distilled. We obtained 3 g of 7-(N-piperidinomethyl)-6-vinyl-1-azabicyclo-(3,2,1)-octane as a mobile colorless liquid, which was soluble in water and organic solvents. The b. p. was 121° (0.35 mm). The substance contained a double bond (test with potassium permanganate).

Found %: C 77.09, 76.78; H 10.77, 10.75. $C_{16}H_{26}N_2$. Calculated %: C 76.92; H 11.12.

Oxidation of 7-(N-piperidinomethyl)-6-vinyl-1-azabicyclo-(3,2,1)-octane. To a solution of 2.3 g of 7-(N-piperidinomethyl)-6-vinyl-1-azabicyclo-(3,2,1)-octane in 23 ml of 10% sulfuric acid was added a solution of 4.15 g of potassium permanganate in 100 ml of water at -2° over a period of 2.5 hours. When the oxidation was complete, the manganese dioxide was removed and washed several times with hot water. The aqueous filtrate was evaporated to small volume, made alkaline with 50% potassium carbonate solution and the unreacted 7-(N-piperidinomethyl)-6-vinyl-1-azabicyclo-(3,2,1)-octane extracted. The alkaline solution was treated with concentrated hydrochloric acid and evaporated to dryness. The dry residue was boiled with 30 ml of an 11% alcohol solution of hydrogen chloride for 4 hours. The alcohol was then evaporated and the residue again heated with an alcohol solution of hydrogen chloride. After removal of the alcohol, the reaction mass was dissolved in 10 ml of water, treated with a 50% solution of potassium carbonate and extracted with ether. The ether solution was dried with potassium carbonate, the solvent removed and the residue vacuum distilled. We obtained 0.5 g of the ethyl ester of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid in the form of a colorless, mobile liquid, which was soluble in organic solvents and had n_D^{18} 1.4909; and b. p. 115° (0.3 mm).

Found %: N 10.31, 10.46. $C_{16}H_{23}O_2N_2$. Calculated %: N 10.00.

The picrate formed yellow crystals, which were soluble in water, alcohol and acetone. The m. p. was 95-100° (decomp.).

Found %: C 45.95, 45.15; H 4.98, 4.72; N 14.80, 14.72. $C_{28}H_{34}O_{16}N_8$. Calculated %: C 45.52; H 4.61; N 15.17.

Hydrazide of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid. A solution of 0.2 g of the ethyl ester of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid and 0.2 ml of hydrazine hydrate in 2 ml of alcohol was boiled for 4 hours. The alcohol and the excess hydrazine hydrate were evaporated in vacuum. The residue, which was an uncrystallizable mass was dissolved in alcohol and added to an alcohol solution of picric acid. We obtained 0.02 g of the tripicrate of the hydrazide of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid as yellow crystals which were soluble in acetone and water and difficultly so in alcohol. The m. p. was 105-108°.

Found %: C 39.69; H 4.15; N 18.88. $C_{32}H_{35}O_{22}N_{13}$. Calculated %: C 40.29; H 3.67; N 19.09.

Hydrochloride of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid. 0.1 g of the ethyl ester of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid and 2 ml of concentrated hydrochloric acid were boiled for 4 hours. The reaction mixture was evaporated to dryness and carefully triturated with ether. We obtained 0.05 g of the hydrochloride of 7-(N-piperidinomethyl)-1-azabicyclo-(3,2,1)-octane-6-carboxylic acid. The colorless crystals were soluble in water and alcohol. The m. p. was 100° (decomp.).

Found %: C 51.63; H 7.64; N 8.95, 8.96. $C_{14}H_{26}O_2N_2Cl_2$. Calculated %: C 51.72; H 8.05; N 8.67.

SUMMARY

1. It was found that distillation of the stearic and benzoic esters of 7-(diethylaminomethyl)-6-(β -hydroxyethyl)-1-azabicyclo-(3,2,1)-octane at atmospheric pressure formed a mixture of equal amounts of 7,6-(3',4'-N-ethylpiperidino)-1-azabicyclo-(3,2,1)-octane and 7-diethylaminomethyl-6-vinyl-1-azabicyclo-(3,2,1)-octane.

2. Distillation of 7-(N-piperidinomethyl)-6-(β -stearoyloxyethyl)-1-azabicyclo-(3,2,1)-octane under the same conditions yielded only one substance, 7-(N-piperidinomethyl)-6-vinyl-1-azabicyclo-(3,2,1)-octane.

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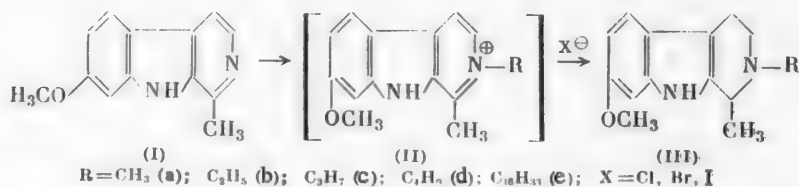
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SYNTHESIS OF PY-N-ALKYLTETRAHYDROHARMINES

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The successful use of reserpine in the treatment of hypertension has recently aroused considerable interest in the synthesis of analogs of this alkaloid. One direction in the search for synthetic analogs of reserpine of simpler structure is the synthesis of β -carboline derivatives [1]. The alkaloid harmine, which is a compound containing the structural elements of the reserpine molecule, was used as the starting material in a series of investigations in this case [2, 3]. Most of the compounds described that were synthesized from harmine were Ind-N-derivatives of harmine. The lack of a satisfactory method of reducing the pyridine ring in harmine hindered the preparation of Py-N-substituted tetrahydro harmine derivatives. Meanwhile, such compounds could be of very great interest as they are closer in structure to reserpine than Ind-N-derivatives of harmine. The convenient method we developed previously [4] for the reduction of harmine derivatives into derivatives of Py-N-tetrahydroharmine with the aid of sodium borohydride made it possible to synthesize the homologous Py-N-alkyltetrahydroharmine, described in the present communication. These compounds were synthesized according to the scheme



Harmine (I) was converted into the Py-quaternary salt (II) by interaction with appropriate alkyl halides. The ease of formation of the quaternary salts changed, depending on the length of the alkyl chain. An increase in the number of carbon atoms in the alkyl chain necessitated more drastic reaction conditions for the preparation of Py-haloalkylates of harmine. While heating in boiling methanol for 2 hours was sufficient for interaction of harmine with methyl iodide [5], the reaction with ethyl iodide required 4 hours' boiling in isopropanol and the reaction with butyl iodide did not proceed in boiling isopropyl alcohol in 5 hours so that the preparation of the Py-N-iodobutylate of harmine (IId) [as in the cases of the Py-N-bromopropylate (IIc) and the Py-N-chlorocetylolate of harmine (Ile)] required heating in benzyl alcohol at 120-130° for 12 hours.

In the interaction of harmine with isopropyl iodide under the same conditions, the formation of only harmine hydroiodide was observed and this was apparently obtained as a result of elimination of hydriodic acid from isopropyl iodide. It is interesting that in analogous cases of the reaction of isopropyl iodide with pyridine [6], α -picoline [7] and isoquinoline [8], the corresponding iodoisopropylates were formed satisfactorily.

The Py-quaternary derivatives of harmine (II) were reduced with sodium borohydride in methanol at room temperature and gave a series of Py-N-alkyltetrahydroharmine (III) [where alkyl = methyl (IIIa), ethyl (IIIb), propyl (IIIc), butyl (IIId) and cetyl (IIIe)] in yields of 87-93%.

EXPERIMENTAL

Py-N-Methyltetrahydroharmine (IIIa). With stirring, 15 g of sodium borohydride was added in portions at no higher than 30° to a mixture of 6 g of harmine iodomethylate, obtained by Fischer and Tauber's method [5],

and 800 ml of methyl alcohol. The whole of the harmine iodomethylate dissolved during the reaction. The reaction was exothermal and was accompanied by frothing of the reaction mass. When all the sodium borohydride had been added, stirring was continued for a further 3 hours. The methanol was then evaporated to 150 ml and the residue obtained diluted with 450 ml of water. The white precipitate was collected, washed with water and dried. The yield of Py-N-methyltetrahydroharmine was 3.63 g (93.2%). The colorless crystals had m. p. 170-172° (from aqueous alcohol). The substance was soluble in methyl alcohol, less soluble in ethyl and isopropyl alcohols, benzene and chloroform and insoluble in ether and water.

Found %: C 72.88, 73.00; H 7.72, 7.82; N 12.19, 11.91. $C_{14}H_{18}ON_2$. Calculated %: C 73.04; H 7.87; N 12.15.

The hydrochloride formed colorless crystals with m. p. 243-244°. The substance was soluble in methanol and water and insoluble in acetone, benzene, chloroform and ether.

Found %: N 10.27, 10.20; Cl' 13.18. $C_{14}H_{18}ON_2$. Calculated %: N 10.49; Cl' 13.28.

Py-N-Iodoethylate of harmine (IIb). 21.22 g of harmine and 31.2 g of ethyl iodide were boiled for 4 hours in 700 ml of isopropyl alcohol. A white crystalline precipitate formed during this process. The reaction mixture was cooled. The precipitate was collected. The yield of the Py-N-iodoethylate of harmine was 31 g (84.3%). The white, crystalline powder had m. p. 258-261° (from water). The substance was soluble in methanol and hot water, sparingly soluble in alcohol, benzene, toluene, chloroform and acetone and insoluble in ether.

Found %: C 48.62; H 4.74; N 7.21; I' 34.06. $C_{15}H_{17}ON_2I$. Calculated %: C 48.90; H 4.66; N 7.61; I' 34.48.

Py-N-Ethyltetrahydroharmine (IIIb). 1 g of the Py-N-iodoethylate of harmine in 200 ml of methyl alcohol was reduced with 2.2 g of sodium borohydride under the conditions described for the preparation of (IIIa). When the reaction was complete, the alcohol was evaporated and the residue extracted with ether. The ether solution was dried with potassium carbonate and the ether removed. We obtained 0.59 g (88.9%) of Py-N-ethyltetrahydroharmine. The colorless crystals had m. p. 112-114° (from aqueous alcohol). The substance was soluble in alcohols, chloroform, benzene and ether and insoluble in cold water.

The hydrochloride formed colorless crystals with m. p. 120-212° (from anhydrous alcohol). The substance was readily soluble in benzene and chloroform, and insoluble in acetone and ether.

Found %: C 63.97; H 7.54; N 10.22; Cl' 12.58, 12.34. $C_{15}H_{20}ON_2 \cdot HCl$. Calculated %: C 64.20; H 7.52; N 9.96; Cl' 12.62.

Py-N-bromopropylate of harmine (IIc). 42.44 g of harmine and 40 g of propyl bromide were heated in 250 ml of benzyl alcohol at 120-130° for 12 hours. The reaction mixture was evaporated at 5-7 mm up to 180°. The residue was triturated with chloroform, collected, washed with chloroform and dried. Recrystallization from absolute alcohol yielded 36.7 g of the Py-N-bromopropylate of harmine. The mother solution yielded a further 17.72 g of Py-N-bromopropylate of harmine after evaporation of part of the alcohol. The total yield was 54.43 g (81.2%). The Py-N-bromopropylate of harmine formed white crystals with m. p. 222-224°. The substance was soluble in alcohols and water and insoluble in benzene, acetone and chloroform.

Found %: C 57.41, 57.70; H 5.40, 5.53; N 8.47; Br' 24.09, 24.05. $C_{16}H_{19}ON_2Br$. Calculated %: C 57.30; H 5.72; N 8.37; Br' 23.83.

Py-N-Propyltetrahydroharmine (IIIc). 25 g of the Py-N-bromopropylate of harmine was reduced with 55 g of sodium borohydride in 1000 ml of methanol under the conditions described in the preparation of (IIIa). After the reaction, the methanol was removed in vacuum. To the residue was added 300 ml of water and the Py-N-propyltetrahydroharmine extracted with ether. The ether solution was dried with potassium carbonate. The ether was evaporated to a volume of 300 ml and then an alcohol solution of hydrogen chloride added to an acid reaction to Congo. The precipitate of Py-N-propyltetrahydroharmine hydrochloride was collected and dried to constant weight in vacuum. The weight was 20 g (91%).

The hydrochloride was a white crystalline powder with m. p. 203-206°. The substance was readily soluble in methanol and less so in ethanol, isopropanol and water. It was difficultly soluble in benzene, chloroform, ether and acetone.

Found %: C 65.54, 65.11; H 7.96, 7.86; N 9.39; Cl' 12.25, 12.23. $C_{16}H_{22}ON_2 \cdot HCl$. Calculated %: C 65.18; H 7.86; N 9.51; Cl' 12.02.

Reaction of harmine with isopropyl iodide. 4.2 g of harmine and 7.36 g of isopropyl iodide were heated at 120-130° in 50 ml of benzyl alcohol for 12 hours. The precipitate which formed when the reaction mixture was cooled was collected and washed with isopropyl alcohol and ether. We obtained 5 g of colorless crystals with m. p. 230-231° (from isopropanol). The substance dissolved on heating in isopropanol and water and was sparingly soluble in methanol and insoluble in acetone, ether, chloroform and benzene. The yield was 73.8%.

Found %: C 45.91, 46.10; H 3.81, 3.57; N 8.19, 8.27; I' 37.45, 37.64. $C_{13}H_{12}ON_2 \cdot HI$. Calculated %: C 45.91; H 3.86; N 8.22; I' 37.30.

According to elementary analysis data, the substance obtained was harmine hydroiodide.

Py-N-Iodobutylate of harmine (IIId) was obtained similarly to the Py-N-bromopropylate of harmine from 30 g of harmine and 40 g of butyl iodide in 250 ml of benzyl alcohol. After evaporation of the reaction mixture at 5-7 mm up to 180°, the residue was triturated with acetone and collected by filtration. The yield of Py-N-iodobutylate of harmine was 47.23 g (84.2%). The white crystalline powder had m. p. 183-184°. The substance was soluble in methyl alcohol. It was less soluble in chloroform, ethanol and acetone, difficultly soluble in benzene and insoluble in ether.

Found %: C 51.57; H 5.38; N 6.98; I' 31.93. $C_{17}H_{21}ON_2I$. Calculated %: C 51.50; H 5.33; N 7.08; I' 32.05.

Py-N-Butyltetrahydroharmine (IIId) was obtained from 39.6 g of the Py-N-iodobutylate of harmine with 60 g of sodium borohydride in 2 liters of methanol under the conditions described for (IIIa). After evaporation of the methanol to 350 ml in vacuum, 1.4 liters of water was added and the precipitate collected and recrystallized from 100 ml of a mixture of methanol and water (3:1). The yield of Py-N-butyltetrahydroharmine was 23.65 g (87%).

The hydrochloride was a light yellow crystalline powder with m. p. 183-186°. The substance was soluble in alcohols and water, difficultly soluble in benzene and acetone and insoluble in ether.

Found %: C 66.28; H 8.35; N 9.45; Cl' 11.58, 11.55. $C_{17}H_{24}ON_2 \cdot HCl$. Calculated %: C 66.11; H 8.16; N 9.07; Cl' 11.48.

The Py-N-chlorocetylrate of harmine (IIe) was obtained similarly to the Py-N-bromopropylate of harmine from 30 g of harmine and 43.6 g of cetyl chloride in 180 ml of benzyl alcohol. After evaporation of the reaction mixture in vacuum, the solid residue was recrystallized from 150 ml of isopropanol. The yield of the Py-N-chlorocetylrate of harmine was 57.6 g (86.4%). The white crystalline powder had m. p. 72-75° (from acetone). The substance was readily soluble in alcohols and chloroform, difficultly soluble in benzene and still less soluble in acetone, ether and water.

Found %: N 5.92, 6.32; Cl' 7.30. $C_{29}H_{45}ON_2Cl$. Calculated %: N 5.92; Cl' 7.49.

Py-N-Cetyl tetrahydroharmine (IIIe). 25 g of the Py-N-chlorocetylrate of harmine was reduced with 40 g of sodium borohydride in 2.5 liters of methanol under the usual conditions. The precipitate formed during the reduction was collected, washed with methanol and dried. We obtained 12 g of Py-N-cetyl tetrahydroharmine. A further 9 g of Py-N-cetyl tetrahydroharmine crystallized from the mother solution after 2.4 liters of methanol had been evaporated and 500 ml of water added. The total yield was 21 g (90.2%).

The hydrochloride formed colorless crystals with m. p. 184-186° (from acetone). The substance was soluble in alcohols and chloroform, and difficultly soluble in acetone, ether and water.

Found %: C 72.92; H 10.40; N 5.73; Cl' 7.37, 7.57. $C_{29}H_{48}ON_2 \cdot HCl$. Calculated %: C 72.99; H 10.35; N 5.87; Cl' 7.43.

SUMMARY

For pharmacological study as analogs of reserpine with a simpler structure, we synthesized Py-N-alkyl tetrahydroharmine with the alkyl residues methyl, ethyl, propyl, butyl and cetyl.

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N-DERIVATIVES OF 2,6-DIMETHYLPYPERIDINE

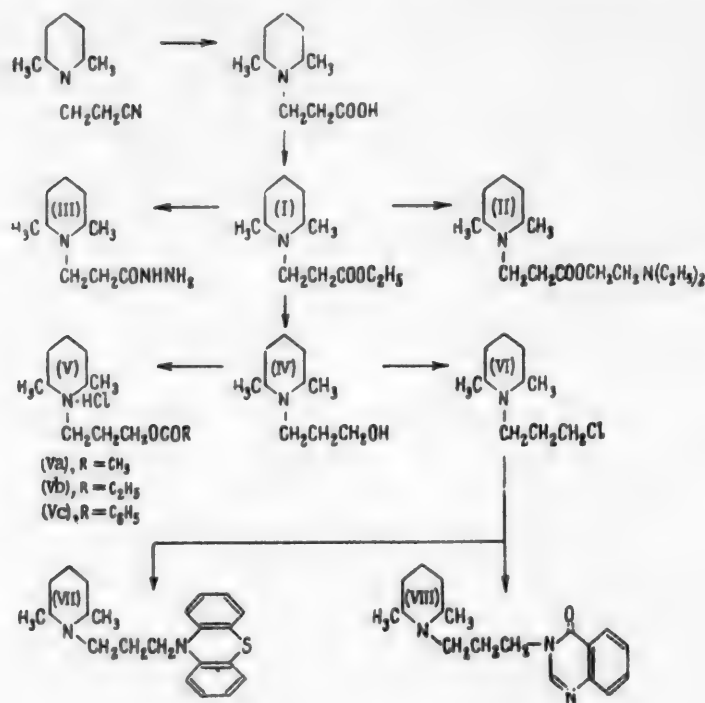
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We showed previously [1] that some derivatives of 1,6-dimethylpiperidine have a high pharmacological activity. Thus, the diiodomethylate of the diethylaminoethyl ester of 1,6-dimethylpipercolinic acid and also 1,6-dimethyl-2-(diethylaminoethylaminomethyl)-piperidine were found to be active ganglion blocking preparations. Continuing the study of methyl derivatives of piperidine, we synthesized a series of N-substituted 2,6-dimethylpiperidines.

In the present work we describe the synthesis of esters of 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine with acetic, propionic and benzoic acids and also of unsymmetrical ditertiary amines containing 2,6-dimethylpiperidine attached through an n-propyl chain to such pharmacologically active heterocyclic systems as phenothiazine and quinosolone.

The starting materials for the synthesis of these substances was 1-(β -cyanoethyl)-2,6-dimethylpiperidine, obtained from 2,6-lutidine, which is a by-product from the production of phthivazide. 2,6-Dimethylpiperidine was cyanoethylated by a method presented in the literature [2]. However, we were unable to achieve the yield reported by these authors. Under the conditions described, 20-30% cyanoethylation occurred instead of the 82%



indicated in the article. When a solution of potassium hydroxide in methyl alcohol was added as a catalyst, the polymerization of acrylonitrile proceeded more rapidly than cyanoethylation and the cyanoethyl derivative was not formed at all. We found that the cyanoethylation reaction proceeded in good yield (80%) when a small amount of water (2%) was added to the reaction mixture.

Further conversions of 1-(β -cyanoethyl)-2,6-dimethylpiperidine were carried out by the above scheme.

Hydrolysis of the cyanoethyl derivative of 2,6-dimethylpiperidine with a mixture of acetic and hydrochloric acids and subsequent esterification of the hydrolysis product with an alcohol solution of hydrogen chloride yielded 1-(β -carboethoxyethyl)-2,6-dimethylpiperidine (I). Transesterification of the latter with diethylaminoethanol in the presence of a small amount of sodium alcoholate gave the diethylaminoethyl ester (II) and interaction with hydrazine hydrate in alcohol gave the hydrazide (III). Reduction of 1-(β -carboethoxyethyl)-2,6-dimethylpiperidine with lithium aluminum hydride in ether solution led to 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine (IV). The latter was esterified by means of the acid chlorides of acetic, propionic and benzoic acids in a benzene medium to form the corresponding ester hydrochlorides (Va), (Vb) and (Vc). Heating 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine with thionyl chloride in chloroform formed 1-(γ -chloropropyl)-2,6-dimethylpiperidine (VI). Reaction of the latter with phenothiazine in benzene in the presence of sodium hydroxide formed 1-[γ -(N-phenothiazino)-propyl]-2,6-dimethylpiperidine (VII) and reaction with the Na salt of quinosolone gave 1-[γ -(3'-quinosolono)-propyl]-2,6-dimethylpiperidine (VIII).

EXPERIMENTAL

1-(β -Cyanoethyl)-2,6-dimethylpiperidine. 8 g of 2,6 dimethylpiperidine was heated on a boiling water bath for 30 hours with 16 ml of acrylonitrile and 0.5 ml of water. At the end of the reaction, the mass was cooled, diluted with 20 ml of benzene and dried with baked sodium sulfate, the benzene removed and the residue vacuum distilled. We obtained 9.39 g (80%) of a colorless, mobile liquid with b. p. 127-129° (29 mm).*

1-(β -Carboethoxyethyl)-2,6-dimethylpiperidine. 16.6 g of 1-(β -cyanoethyl)-2,6-dimethylpiperidine, 166 ml of concentrated hydrochloric acid and 332 ml of glacial acetic acid were boiled for 30 hours. The reaction mixture was evaporated to dryness. We obtained 26.6 g of a mixture of the hydrochloride of 1-(β -carboxyethyl)-2,6-dimethylpiperidine and ammonium chloride. The mixture was boiled on a water bath for 4 hours with a 10-fold amount of a 10% alcohol solution of hydrogen chloride. The solution was filtered free from ammonium chloride in the hot and evaporated in vacuum and the residue again boiled for 4 hours with a 10-fold amount of a 10% alcohol solution of hydrogen chloride. The alcohol was removed in vacuum and the residue treated with excess 50% potassium carbonate solution and extracted with ether. The ether extract was dried with baked sodium sulfate, the ether removed and the residue vacuum distilled. We obtained 13.4 g (62.8%) of a colorless, mobile liquid with b. p. 72-73° (0.3 mm).

Found %: C 67.90; H 11.00; N 6.67. $C_{12}H_{23}O_2N$. Calculated %: C 67.60; H 10.79; N 6.57.

To isolate the hydrochloride of the acid, free from inorganic salts, 0.32 g of the ester was hydrolyzed by boiling with 5 ml of dilute (1:1) hydrochloric acid for 4 hours. The solution formed was evaporated to a thick, pasty mass in a porcelain dish, treated with 5 ml of anhydrous acetone and filtered. We obtained 0.33 g of a white crystalline substance with m. p. 188-189°.

Found %: N 6.30; Cl 16.08. $C_{10}H_{20}O_2NCl$. Calculated %: N 6.32; Cl 16.03.

Diethylaminoethyl ester of 1-(β -carboxyethyl)-2,6-dimethylpiperidine. 0.22 g of sodium was dissolved in 40 ml of diethylaminoethanol. To the solution formed was added 4.27 g of 1-(β -carboethoxyethyl)-2,6-dimethylpiperidine and the reaction mixture heated at 155-160° for 4 hours, while the alcohol distilled. At the end of the reaction the excess diethylaminoethanol was removed in vacuum. The residue was treated with excess 50% potassium carbonate solution and extracted with ether. The ether was dried with anhydrous sodium sulfate and removed. The residue was vacuum distilled. We obtained 2.43 g (44%) of the diethylaminoethyl ester of 1-(β -carboxyethyl)-2,6-dimethylpiperidine as a light yellow, oily liquid with b. p. 160-162° (0.3 mm).

Found %: C 63.90; H 10.77; N 10.15. $C_{16}H_{32}O_2N_2$. Calculated %: C 64.08; H 11.26; N 9.85.

Hydrazide of 1-(β -carboxyethyl)-2,6-dimethylpiperidine. 1 g of 1-(β -carboethoxyethyl)-2,6-dimethylpiperidine, 0.73 g of 65% hydrazine hydrate and 1.5 ml of anhydrous alcohol were boiled for 3 hours. The alcohol

* According to literature data: b.p. 121-126° (26-28 mm) [2].

was removed in vacuum and the residue crystallized on standing. We obtained 0.9 g (96%) of a crystalline substance with m. p. 77-79° (from ligroine).

Found %: C 59.78; H 10.28; N 21.65. $C_{10}H_{21}ON_2$. Calculated %: C 60.30; H 10.55; N 21.10.

1-(γ -Hydroxypropyl)-2,6-dimethylpiperidine. 3.97 g of 1-(β -carbethoxyethyl)-2,6-dimethylpiperidine was reduced with 1.06 g of lithium aluminum hydride in 50 ml of anhydrous ether for 4 hours. We obtained 2.67 g (83%) of a colorless, immobile liquid with b. p. 101-102° (0.5 mm).

Found %: C 70.05; H 12.06; N 8.17. $C_{10}H_{21}ON$. Calculated %: C 70.17; H 12.28; N 8.18.

The iodomethylate was a white crystalline substance with m. p. 224-225°.

Found %: N 4.24; I 40.85. $C_{11}H_{24}ONI$. Calculated %: N 4.47; I 40.54.

The hydrochloride was a white crystalline substance with m. p. 130-132°.

Found %: N 6.83; Cl 16.88. $C_{10}H_{22}ONCl$. Calculated %: N 6.74; Cl 17.10.

Hydrochloride of 1-(γ benzoyloxypropyl)-2,6-dimethylpiperidine. 1.25 g of 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine and 1.53 g of benzoyl chloride were boiled for 3 hours in 15 ml of dry benzene. The reaction mixture was cooled and the precipitate collected and reprecipitated from anhydrous alcohol with ether. We obtained 1.92 g (84%) of a white crystalline substance with m. p. 169-170°.

Found %: N 4.73; Cl 11.25. $C_{17}H_{26}O_2NCl$. Calculated %: N 4.49; Cl 11.39.

Hydrochloride of 1-(γ -acetoxypropyl)-2,6-dimethylpiperidine. 1.3 g of 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine and 1.2 g of acetyl chloride were boiled for 3 hours in 10 ml of anhydrous benzene. After the reaction, the benzene was removed in vacuum and the residue triturated with anhydrous ether, collected by filtration and reprecipitated from anhydrous alcohol with ether. We obtained 1.24 g (65%) of a white crystalline substance with m. p. 117-119°.

Found %: N 5.81; Cl 13.97. $C_{12}H_{24}O_2NCl$. Calculated %: N 5.61; Cl 14.22.

Hydrochloride of 1-(γ -propionyloxypropyl)-2,6-dimethylpiperidine. By the method described above, from 1.6 g of 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine and 1.61 g of propionyl chloride in 15 ml of anhydrous benzene we obtained 1.77 g (73%) of a white crystalline substance with m. p. 102-104°.

Found %: N 5.25; Cl 13.27. $C_{13}H_{26}O_2NCl$. Calculated %: N 5.31; Cl 13.47.

1-(γ -chloropropyl)-2,6-dimethylpiperidine. 0.84 g of the hydrochloride of 1-(γ -hydroxypropyl)-2,6-dimethylpiperidine, 3.5 ml of chloroform and 3.5 ml of thionyl chloride were heated at 50° for 10 minutes. The solution was evaporated in vacuum, anhydrous ether added to the residue, and the precipitate formed was collected and reprecipitated from anhydrous alcohol with ether. We obtained 0.71 g (78%) of a white crystalline substance with m. p. 171-172°.

Found %: N 6.29; Cl 31.22. $C_{10}H_{21}NCl_2$. Calculated %: N 6.19; Cl 31.41.

The hydrochloride was treated with excess 50% potassium carbonate solution and extracted with ether. The ether extract was dried with anhydrous sodium sulfate, the ether removed and the residue vacuum distilled. We obtained a substance with b. p. 63° (0.5 mm) as a colorless, oily liquid.

Found %: N 7.28; Cl 18.44. $C_{10}H_{20}NCl$. Calculated %: N 7.38; Cl 18.74.

1-[γ -(N-Phenothiazino)-propyl]-2,6-dimethylpiperidine. Into a flask fitted with a Dean and Stark head and a reflux condenser were placed 3.67 g of the hydrochloride of 1-(γ -chloropropyl)-2,6-dimethylpiperidine, 2.15 g of phenothiazine, 1.73 of sodium hydroxide and 15 ml of anhydrous benzene. The reaction mixture was heated on a boiling water bath until the distillation of water ceased (4-6 hours). The benzene was removed, the residue treated with excess 5% hydrochloric acid and the precipitate formed was collected and washed with water. The aqueous acid mother solutions were made alkaline with 40% sodium hydroxide and extracted with ether. The ether was dried with anhydrous sodium sulfate and evaporated. The residue was vacuum distilled. We obtained 1.34 g of the original base chloride with b. p. 68-69° (0.7 mm), giving a hydrochloride with m. p. 171-172°. The precipitate collected from the acid mother solution was carefully washed with ether and then with acetone

and finally reprecipitated from anhydrous alcohol with ether. We obtained 1 g (23.8%) of a yellowish green, finely crystalline substance with m. p. 253.5-255.5°.

Found %: N 7.58; Cl 9.16. $C_{22}H_{29}N_2SCl$. Calculated %: N 7.20; Cl 9.13.

Dihydrochloride of 1-[γ -(3'-quinosolono)-propyl]-2,6-dimethylpiperidine. 0.46 g of metallic sodium was dissolved in 15 ml of anhydrous alcohol. To the warm solution was added 2.92 g of quinosolone and the mixture shaken. To the dark brown solution formed was added a solution of 3.8 g of 1-(γ -chloropropyl)-2,6-dimethylpiperidine in 10 ml of anhydrous alcohol. The reaction mixture was boiled until the alkaline reaction disappeared (10-12 hours), then the alcohol removed in vacuum, the residue made acid to Congo with 5% hydrochloric acid, the solution formed shaken twice with 30 ml of ether and the aqueous solution separated, made alkaline with 40% sodium hydroxide solution and extracted with ether. The ether extract was dried with baked sodium sulfate, filtered and acidified with an alcohol solution of hydrogen chloride. We obtained 4.3 g (58%) of the dihydrochloride of 1-[γ -(3'-quinosolono)-propyl]-2,6-dimethylpiperidine as a white, hygroscopic crystalline substance with m. p. 216.5-218.5° (reprecipitated from anhydrous alcohol with ether). The substance contained 1 mole of water of crystallization.

Found %: N 10.72; Cl 18.40. $C_{18}H_{27}ON_2Cl_2 \cdot H_2O$. Calculated %: N 10.76; Cl 18.20.

SUMMARY

Some N-substituted 2,6-dimethylpiperidines were synthesized so that they could be studied pharmacologically.

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ADDITION OF FULL ESTERS OF PHOSPHOROUS AND PHOSPHINOUS ACIDS TO CONJUGATED SYSTEMS

VIII. INTERACTION OF ETHYLPHOSPHINOUS ESTERS WITH ACRYLIC AND METHACRYLIC ACIDS

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The purpose of this work was to study the interaction of esters of ethylphosphinous acid with acrylic and methacrylic acids. These reactions are analogous in mechanism to the reaction of α,β -unsaturated acids with trialkyl phosphites and esters of phenylphosphinous acids, described in previous communications [1, 2]. In one of these [2], it was established that esters of phenylphosphinous acid react more actively than trialkyl phosphites, not only with alkyl halides, but also with π,π -conjugated systems. Therefore, it was to be expected that esters of ethylphosphinous acid would also react readily with α,β -unsaturated acids.

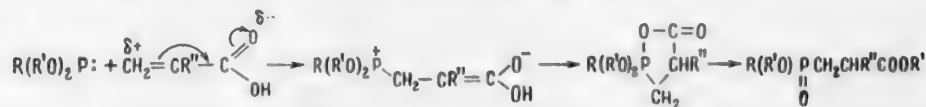
In fact, our experiments showed that esters of ethylphosphinous acid interact with acrylic and methacrylic acids more actively than trialkyl phosphites or esters of phenylphosphinous acid. Even after the addition of the first three drops of acrylic acid to ethyl ethylphosphinite, the temperature rose to 90° and further addition of acrylic acid was carried out with cooling in ice. The reaction proceeds more smoothly in an ether medium. Methacrylic acid reacts with esters of ethylphosphinous acid less vigorously.

Substance	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR _D		% P		Yield (in %)
				found	calc.	found	calc.	
$\begin{array}{c} \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5\text{O} \end{array} \text{P} \begin{array}{c} \text{O} \\ \text{CH}_2\text{CH}_2\text{COOC}_2\text{H}_5 \end{array}$	114—115 (2)	1.4450	1.0810	54.16	54.76	14.33	14.48	36.7
$\begin{array}{c} \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5\text{C} \end{array} \text{P} \begin{array}{c} \text{O} \\ \text{CH}_2\text{CHCOOC}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	139—140 (5)	1.4440	1.0575	59.28	59.38	*	—	40.5
$\begin{array}{c} \text{C}_2\text{H}_5 \\ n\text{-C}_2\text{H}_5\text{O} \end{array} \text{P} \begin{array}{c} \text{O} \\ \text{CH}_2\text{CH}_2\text{COOC}_2\text{H}_5 \end{array}$	143—145 (3)	1.4455	—	—	—	12.01	12.40	25
$\begin{array}{c} \text{C}_2\text{H}_5 \\ n\text{-C}_2\text{H}_5\text{O} \end{array} \text{P} \begin{array}{c} \text{O} \\ \text{CH}_2\text{CHCOOC}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	141 (3)	1.4470	1.0417	67.82	68.61	11.39	11.75	27
$\begin{array}{c} \text{C}_2\text{H}_5 \\ n\text{-C}_2\text{H}_5\text{O} \end{array} \text{P} \begin{array}{c} \text{O} \\ \text{CH}_2\text{CH}_2\text{COOC}_2\text{H}_5 \end{array}$	157—159 (3)	1.4510	1.0199	73.41	73.32	*	—	46
$\begin{array}{c} \text{C}_2\text{H}_5 \\ n\text{-C}_2\text{H}_5\text{O} \end{array} \text{P} \begin{array}{c} \text{O} \\ \text{CH}_2\text{CHCOOC}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	151—152 (3)	1.4510	1.0094	77.89	77.65	*	—	50

* The constants are identical with those given previously in the literature [3].

It should be noted that the ethyl ester of ethylphosphinous acid reacts with acrylic and methacrylic acids more vigorously than the n-propyl and n-butyl ester. Thus, the reactivity of various esters of ethylphosphinous acids with respect to α,β -unsaturated acids also depends on the size of the radical as in other cases of Arbuzov rearrangement.

The reactions we studied evidently proceed according to the scheme



We were unable to prove that the intermediate products of the Arbuzov rearrangement were formed in this reaction, probably because the interaction of α,β -unsaturated acids with esters of ethylphosphinous acid proceeds more vigorously than with trialkyl phosphites. The constants of the compounds obtained are given in the table.

EXPERIMENTAL

Addition of ethyl ethylphosphinite to acrylic acid. With cooling, 5.1 g of acrylic acid was added to 9.4 g of ethyl ethylphosphinite in ether. The reaction mixture was then heated for 3 hours on a water bath. The reaction was performed in a stream of carbon dioxide. After removal of the ether, the residue was vacuum distilled. We obtained 5.3 g (36.7%) of the diethyl ester of β -ethylphosphonopropionic acid.

B. p. 114-115° (2 mm), n_D^{20} 1.4450, d_4^{20} 1.0810; MR_D 54.16; Calc. 54.76. Found %: P 14.33. $C_9H_{19}O_4P$. Calculated %: P 14.48.

The reactions of acrylic acid with other esters of ethylphosphinic acid were carried out in the same way.

Addition of ethyl ethylphosphinite to methacrylic acid. 8 g of methacrylic acid was added dropwise to 12.5 g of ethyl ethylphosphinite. When about 1 g of acid had been added, the reaction flask was placed for a few seconds in a water bath at 45°. The temperature of the mixture rapidly rose to 60°, continued to rise when heating was stopped and reached 110°. The rest of the methacrylic acid was added with the reaction flask cooled in ice water. When the mixture had cooled to room temperature, the flask was again heated to 80-90° for 1.5 hours. The reaction was performed under carbon dioxide. Vacuum distillation yielded 8.3 g (40.5%) of the diethyl ester of β -ethylphosphonoisobutyric acid.

B. p. 139-140° (5 mm), n_D^{20} 1.4440, d_4^{20} 1.0575, MR 59.28; Calc. 59.38.

Literature data [3]: b. p. 108-109° (0.5 mm), n_D^{20} 1.4420, d_4^{20} 1.0530.

Methacrylic acid was reacted with other esters of ethyl phosphinous acid in the same way.

SUMMARY

The interaction of esters of ethylphosphinous acid with acrylic and methacrylic acids was studied. It was established that esters of alkylphosphinous acids react with α,β -unsaturated acids more actively than trialkyl phosphites.

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INTERACTION OF POTASSIUM ACETATE WITH β -CHLOROKETONES

ADDITION OF CARBOXYLIC ACIDS TO VINYL KETONES

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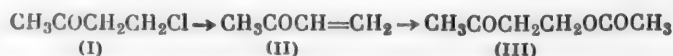
Moscow State University

It was previously found [1] that 1-chloro-4-acetoxybutanone-2 was formed during the action of potassium acetate in acetic acid on 1,4-dichlorobutanone-2 at room temperature. It was shown that the reaction proceeded through the intermediate formation of chloromethyl vinyl ketone with subsequent addition of acetic acid to the latter under the catalytic effect of potassium acetate.

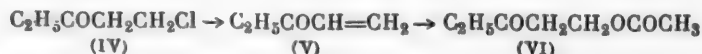
It was then found that when a mixture of 1-chloro-4-acetoxybutanone-2 and 1,1'-dicyclohexenyl was heated in the presence of potassium acetate, the product of the addition of chloromethyl vinyl ketone to 1,1'-dicyclohexenyl was formed. Consequently, 1-chloro-4-acetoxybutanone-2 decomposes to chloromethyl vinyl ketone and acetic acid when heated in the presence of potassium acetate.

In the present work the interaction of 4-chlorobutanone-2 and 5-chloropentanone-3 with potassium acetate in acetic acid was studied and the addition of carboxylic acids to methyl vinyl and ethyl vinyl ketones was investigated.

The reaction between 4-chlorobutanone-2 (I) and potassium acetate in acetic acid at room temperature formed 4-acetoxybutanone-2 (III).



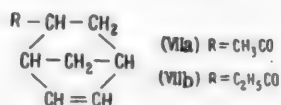
The action of potassium acetate in acetic acid on 5-chloropentanone-3 (IV) at room temperature yielded 5-acetoxypentanone-3 (VI).



Assuming that under these conditions the reaction proceeds through the intermediate formation of the vinyl ketones (II) and (V), we investigated the capacity of potassium acetate to cleave hydrogen chloride from 4-chlorobutanone-2 and 5-chloropentanone-3 and the reaction of acetic acid with methyl vinyl and ethyl vinyl ketones.

By the action of potassium acetate of 4-chlorobutanone-2 (I) and 5-chloropentanone-3 (IV) in an ethanol medium in the presence of cyclopentadiene we obtained 1-acetyl-2,5-endomethylenecyclohexene-3 (VIIa) and 1-propionyl-2,5-endomethylenecyclohexene-3 (VIIb), respectively.

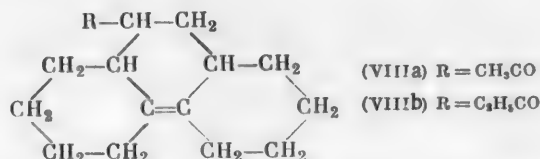
Consequently, potassium acetate cleaves hydrogen chloride from β -chloroketones (I) and (IV) with the formation of vinyl ketones (II) and (V).



It was then necessary to determine whether methyl vinyl and ethyl vinyl ketones added acetic acid.

It was found that in the presence of potassium acetate, acetic acid reacted with methyl vinyl ketone (II) and ethyl vinyl ketone (V) even at room temperature to form 4-acetoxybutanone-2 (III) and 5-acetoxypentanone-3 (VI), respectively. Ethyl vinyl ketone was also capable of adding acetic acid in the absence of potassium acetate. However, under these conditions the reaction proceeded very slowly.

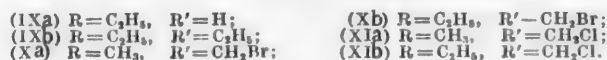
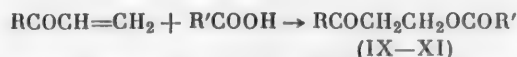
It was found [2] that acetic acid adds to methyl vinyl ketone in the presence of mercury acetate with heating. We found that this reaction proceeds even at room temperature. Then it was established that heating mixtures of 4-acetoxybutanone-2 and 5-acetoxypentanone-3 with 1,1'-dicyclohexenyl in the presence of potassium acetate at 125° formed 1-acetyl-2,3,4,5-dicyclohexanocyclohexene-3 (VIIIa) and 1-propionyl-2,3,4,5-dicyclohexanocyclohexene-3 (VIIIb), respectively.



Thus, it was shown that β -acetoxyketones can split out acetic acid when heated in the presence of potassium acetate.

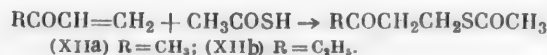
From what has been said it follows that an equilibrium is established in the presence of potassium acetate between vinyl ketones and acetic acid, on one hand, and β -acetoxyketones, on the other. With an increase in temperature, this equilibrium is displaced toward the formation of vinyl ketones and acetic acid.

Then we added a series of carboxylic acids to methyl vinyl and ethyl vinyl ketones.



Formic and propionic acids added to ethyl vinyl ketone at room temperature in the presence of potassium salts of the corresponding acids to form 5-formoxypentanone-3 (IXa) and 5-propoxypentanone-3 (IXb). Under the same conditions, bromoacetic and chloroacetic acids added to methyl vinyl and ethyl vinyl ketones to form 4-bromoacetoxybutanone-2 (Xa), 5-bromoacetoxybutanone-3 (Xb), 4-chloroacetoxybutanone-2 (XIa) and 5-chloroacetoxybutanone-3 (XIb), respectively.

Thioacetic acid reacted with methyl vinyl and ethyl vinyl ketones to form 4-thioacetoxybutanone-2 (XIIa) and 5-thioacetoxybutanone-3 (XIIb).



EXPERIMENTAL

Preparation of 4-chlorobutanone-2 (I). Into a flask fitted with a stirrer, dropping funnel and gas inlet and outlet tubes were placed 133.5 g of aluminum chloride and 350 ml of dry 1,2-dichloroethane. 78.5 g of acetyl chloride was added over a period of 10 minutes. After solution of the aluminum chloride, the mixture was cooled to room temperature and the input of dry ethylene was begun. After some time the temperature began to rise and the flask was cooled with a mixture of ice and salt. The ethylene was passed for 5 hours, while the temperature of the mixture was kept within the range of 0 to +5°. The reaction mixture was then poured with stirring into a mixture of hydrochloric acid and crushed ice at such a rate that the temperature did not rise above 20°. The organic layer was separated and washed with 10% hydrochloric acid and water and the aqueous layer extracted with ether. The ether extracts were added to the organic layer and the solution dried with MgSO₄. The ether and

dichloroethane were removed under reduced pressure and the residue vacuum distilled. We obtained 61.8 g (58%) of 4-chlorobutanone-2 with b. p. 47-49° (16 mm). After a second distillation, the substance had b. p. 41-43° (10 mm), d_4^{20} 1.0697, n_D^{20} 1.4334 [3-5].

Preparation of methyl vinyl ketone (II). Into a flask fitted with a dropping funnel and a short fractionating column were placed 68 g of sodium benzoate and 150 ml of water. The solution was heated to boiling on an oil bath and over a period of 15 minutes, 30 g of 4-chlorobutanone-2 was added to the boiling solution. The temperature of the bath was kept at 140-150°. When the temperature of the emergent vapors reached 99°, the distillation was stopped. The distillate was saturated with $(NH_4)_2SO_4$ and the organic layer separated from the aqueous one and dried with Na_2SO_4 . We obtained 15.2 g (77%) of methyl vinyl ketone with b. p. 76-82°. After a second distillation, the substance had b. p. 78-82°, d_4^{20} 0.8524, n_D^{20} 1.4103 [6,7].

Preparation of 5-chloropentanone-3 (IV). Into a flask fitted with a stirrer, thermometer and inlet and outlet tubes were placed 245 g of propionyl chloride and 450 ml of dry 1,2-dichloroethane. 355 g of aluminum chloride was introduced into the flask with stirring. When the aluminum chloride had dissolved, the mixture was cooled to room temperature and dry ethylene passed through for 6 hours. The temperature of the mixture was kept within the range of from -7 to -3° by cooling the flask with a mixture of ice and salt. The reaction mixture was then treated as in the preparation of 4-chlorobutanone-2. We obtained 182 g (57%) of 5-chloropentanone-3 with b. p. 54-59° (20 mm). After redistillation, the substance had b. p. 42-43° (9 mm), d_4^{20} 1.0458, n_D^{20} 1.4362 [8, 9].

Preparation of ethyl vinyl ketone (V). Into a flask fitted with dropping funnel and a short fractionating column was placed a solution of 100 g of sodium benzoate in 250 ml of water. The solution was heated to boiling and over a period of 25 minutes, 50 g (0.41 mole) of 5-chloropentanone-3 was added to the boiling solution. The temperature of the bath was kept within the range 145-150°. Distillation was stopped when the temperature of the emergent vapors reached 99°. Processing in the usual way yielded 24.2 g (70%) of ethyl vinyl ketone with b. p. 45-47° (100 mm). After redistillation, the substance had b. p. 44-45° (95 mm), d_4^{20} 0.8473, n_D^{20} 1.4202 [8-10].

Addition of acetic acid to methyl vinyl ketone at room temperature in the presence of potassium acetate. To a solution of 1.95 g of anhydrous potassium acetate in 39 g of glacial acetic acid was added 15.2 g of methyl vinyl ketone. The mixture was left for 14 days. It was then poured into water and neutralized with $NaHCO_3$. The organic layer was separated and the aqueous layer extracted with ether. The ether extracts were combined with the organic layer and the solution dried with Na_2SO_4 . We obtained 21 g (74%) of 4-acetoxybutanone-2 (III) with b. p. 78-79° (10 mm). Redistillation gave a substance with b. p. 77-78° (9 mm), d_4^{20} 1.0421, n_D^{20} 1.4203. Semicarbazone: m. p. 135.5-136.5° (from benzene) [2, 11, 12].

Addition of acetic acid to methyl vinyl ketone at room temperature in the presence of mercury acetate. A mixture of 10.5 g of methyl vinyl ketone, 3.8 g of mercury acetate and 27 g of glacial acetic acid was left for 6 days. It was then poured into water, neutralized with $NaHCO_3$ and extracted with ether. We obtained 4.4 g (23%) of 4-acetoxybutanone-2 with b. p. 78-79° (9 mm) and n_D^{20} 1.4212.

Addition of acetic acid to methyl vinyl ketone with heating in the presence of mercury acetate. A mixture of 8.8 g of methyl vinyl ketone, 3.2 g of mercury acetate and 22.5 g of glacial acetic acid was heated for 5 hours on a boiling water bath. We obtained 6.3 g (38%) of 4-acetoxybutanone-2 with b. p. 77-78° (9 mm) and n_D^{20} 1.4209.

Interaction of 4-chlorobutanone-2 with potassium acetate in acetic acid. To a solution of 29.4 g of anhydrous potassium acetate in 90 g glacial acetic acid was added 31.9 g of 4-chlorobutanone-2. After several minutes the separation of KCl began. The mixture was left for 30 days. The usual processing yielded 24.9 g (64%) of 4-acetoxybutanone-2 with b. p. 82-83° (12 mm) and n_D^{20} 1.4210.

Addition of acetic acid to ethyl vinyl ketone at room temperature in the presence of potassium acetate. A mixture of 19.7 g of ethyl vinyl ketone, 2.5 g of anhydrous potassium acetate and 28.1 g of glacial acetic acid was left for 6 days. The usual processing yielded 25.0 g (74%) of 5-acetoxypentanone-3 with b. p. 89-90° (11 mm), d_4^{20} 1.0218, n_D^{20} 1.4318.

Found %: C 58.42, 58.39; H 8.53, 8.58. $C_7H_{12}O_3$. Calculated %: C 58.31; H 8.39.

Semicarbazone: m. p. 110-110.5° (from benzene).

Found %: C 47.70, 47.53; H 7.61, 7.55; N 20.91, 20.86. $C_8H_{15}O_3N_3$. Calculated %: C 47.75; H 7.51; N 20.88.

Addition of acetic acid to ethyl vinyl ketone at room temperature without catalyst. A mixture of 13.9 g of ethyl vinyl ketone and 20 g of glacial acetic acid was sealed in an ampoule and left for 45 days. We obtained 4.5 g (19%) of 5-acetoxypentanone-3 with b. p. 92-94° (13 mm) and n_D^{20} 1.4297.

Addition of acetic acid to ethyl vinyl ketone with heating without catalyst. A mixture of 19.5 g of ethyl vinyl ketone and 41 g of glacial acetic acid was heated on a boiling water bath for 6 hours. We obtained 9.7 g (29%) of 5-acetoxypentanone-3 with b. p. 99-101° (17 mm) and n_D^{20} 1.4304.

Interaction of 5-chloropentanone-3 (IV) with potassium acetate in acetic acid. To a solution of 16.2 g of potassium acetate in 60 ml (1 mole) of glacial acetic acid was added 20 g of 5-chloropentanone-3. Even after a few minutes, the precipitation of KCl began. The mixture was left for 14 days. The normal processing yielded 18.3 g (77%) of 5-acetoxypentanone-3 with b. p. 80-82° (8 mm) and n_D^{20} 1.4285.

Addition of formic acid to ethyl vinyl ketone. A mixture of 21 g of ethyl vinyl ketone, 2.1 g of potassium formate and 23 g of anhydrous formic acid was left for 6 days. The normal processing yielded 22.6 g (74%) of 5-formoxypentanone-3 (IXa) with b. p. 84-85° (11 mm). After redistillation, the substance had b. p. 80-81° (10 mm), d_4^{20} 1.0538, n_D^{20} 1.4276.

Found %: C 55.65, 55.46; H 7.94, 7.91. $C_6H_{10}O_3$. Calculated %: C 55.37; H 7.75.

Semicarbazone: m. p. 98° (from benzene).

Found %: C 44.94, 45.04; H 7.15, 7.26; N 22.32, 22.12. $C_7H_{13}O_3N_3$. Calculated %: C 44.91; H 7.00; N 22.45.

Addition of propionic acid to ethyl vinyl ketone. 1.38 g of potassium carbonate was mixed with 22.4 g of anhydrous propionic acid and 13.1 g of ethyl vinyl ketone, after which the mixture was left for 6 days. The usual processing yielded 17.5 g (71%) of 5-propoxypentanone-3 (IXb) with b. p. 95-98° (11 mm). After redistillation the substance had b. p. 96-97° (11 mm), d_4^{20} 1.0013, n_D^{20} 1.4270.

Found %: C 60.62, 60.64; H 9.16, 9.02. $C_8H_{14}O_3$. Calculated %: C 60.74; H 8.92.

Semicarbazone: m. p. 115-115.5° (from benzene).

Found %: C 50.28, 50.40; H 8.04, 7.98; N 19.17, 18.94. $C_9H_{17}O_3N_3$. Calculated %: C 50.22; H 7.96; N 19.52.

Addition of bromoacetic acid to methyl vinyl ketone. A mixture of 37.0 g of bromoacetic acid and 2.35 g of potassium bromoacetate was heated until the bromoacetic acid melted and then 9.3 g of methyl vinyl ketone was added to it. The mixture was stirred and left for 6 days. The usual processing yielded 18.9 g (68%) of 4-bromoacetoxypentanone-2 (Xa) with b. p. 117-119° (9 mm). After redistillation, the substance had b. p. 105-107° (6 mm), d_4^{20} 1.5173, n_D^{20} 1.4745.

Found %: C 34.51, 34.58; H 4.41, 4.45; Br 38.09, 37.84. $C_6H_9O_3Br$. Calculated %: C 34.47; H 4.34; Br 38.22.

Addition of bromoacetic acid to ethyl vinyl ketone. A mixture of 25.0 g of bromoacetic acid and 1.8 g of potassium bromoacetate was heated until the bromoacetic acid melted. Then 9.9 g of ethyl vinyl ketone was added and the mixture stirred and left for 6 days. The usual processing yielded 18.9 g (72%) of 5-bromoacetoxypentanone-3 (Xb) with b. p. 136-138° (12 mm). After redistillation, the substance had b. p. 128-129° (8 mm), d_4^{20} 1.4494, n_D^{20} 1.4730.

Found %: C 37.53, 37.53; H 5.16, 5.01; Br 35.43, 35.50. $C_7H_{11}O_3Br$. Calculated %: C 37.68; H 4.97; Br 35.85.

Addition of chloroacetic acid to methyl vinyl ketone. To 18.9 g of molten chloroacetic acid was added 1.38 g of potassium carbonate and 7.0 g of methyl vinyl ketone. The mixture was left for 12 days. The usual processing yielded 8.4 g (51%) of 4-chloroacetoxypentanone-2 (XIa) with b. p. 88-89° (2.5 mm), d_4^{20} 1.2180, n_D^{20} 1.4528.

Found %: C 43.43, 43.50; H 5.54, 5.52; Cl 21.59, 21.33. $C_6H_9O_3Cl$. Calculated %: C 43.78; H 5.51; Cl 21.54.

Addition of chloroacetic acid to ethyl vinyl ketone. 18.9 g of molten chloroacetic acid was mixed with 1.38 g of potassium carbonate and 8.4 g of ethyl vinyl ketone. The mixture was left for 14 days. The usual processing yielded 11.0 g (62%) of 5-chloroacetoxypentanone-3 (XIb) with b. p. 95-96° (3 mm), d_4^{20} 1.1816, n_D^{20} 1.4537.

Found %: C 47.41, 47.31; H 6.65, 6.68; Cl 19.88, 20.22. $C_7H_{11}O_2Cl$. Calculated %: C 47.01; H 6.21; Cl 19.85.

Semicarbazone: m. p. 98-98.5° (from benzene).

Found %: C 40.92, 41.01; H 5.97, 6.09; N 17.62, 17.56. $C_8H_{14}O_2N_2Cl$. Calculated %: C 40.77; H 5.89; N 17.83.

Addition of thioacetic acid to methyl vinyl ketone. Into a flask fitted with a reflux condenser was placed 9.0 g of methyl vinyl ketone. The flask was cooled with ice. 19.5 g of thioacetic acid was added dropwise through the condenser. The mixture was left for 1 hour and then vacuum distilled. We obtained 17.0 g (91%) of 4-thioacetoxypentanone-2 (XIIa) with b. p. 92-92.5° (8 mm), d_4^{20} 1.0917, n_D^{20} 1.4824.

Found %: C 49.38, 49.45; H 7.00, 7.07. $C_6H_{10}O_2S$. Calculated %: C 49.31; H 6.90.

Semicarbazone: m. p. 138.5-139° (from benzene).

Found %: C 41.10, 41.23; H 6.33, 6.41; N 20.76, 20.67; S 15.59, 15.65. $C_7H_{12}O_2N_2S$. Calculated %: C 41.31; H 6.45; N 20.68; S 15.75.

Addition of thioacetic acid to ethyl vinyl ketone. Into a flask fitted with a reflux condenser and cooled in ice was placed 10.0 g of ethyl vinyl ketone. 18.1 g of thioacetic acid was added dropwise through the reflux condenser. The mixture was left for 2 days. Vacuum distillation yielded 17.2 g (90%) of 5-thioacetoxypentanone-3 (XIIb) with b. p. 98-99° (7 mm), d_4^{20} 1.0649, n_D^{20} 1.4825.

Found %: C 52.77, 52.62; H 7.73, 7.74. $C_7H_{12}O_2S$. Calculated %: C 52.49; H 7.55.

Semicarbazone: m. p. 125.5-126° (from benzene).

Found %: C 44.04, 44.03; H 6.91, 6.89; N 19.27, 19.31; S 14.51, 14.73. $C_8H_{15}O_2N_2S$. Calculated %: C 44.23; H 6.96; N 19.35; S 14.73.

Preparation of 1-acetyl-2,5-endomethylenecyclohexene-3 (VIIa) from 4-chlorobutanone-2, potassium acetate and cyclopentadiene. Into a flask fitted with a reflux condenser was placed a solution of 10.65 g of 4-chlorobutanone-2 and 9.8 g of potassium acetate in 60 ml of 95% ethanol. Through the condenser was added 9.9 g of cyclopentadiene. Almost immediately the separation of KCl began and the solution evolved heat. The mixture was left for 1.5 hours and then heated on a water bath for 2 hours. The KCl was collected, the ethanol removed in vacuum and the residue poured into water, neutralized with $NaHCO_3$ and extracted with ether. The ether extracts were dried with $CaCl_2$. We obtained 10.8 g (80%) of 1-acetyl-2,5-endomethylenecyclohexene-3 with b. p. 66-67° (9 mm), d_4^{20} 1.0064, n_D^{20} 1.4853.

Semicarbazone: m. p. 166.5-167° (from ethanol) [13, 14].

Reaction of ethyl vinyl ketone with cyclopentadiene. Into a flask fitted with a reflux condenser was placed 8.4 g of ethyl vinyl ketone and 9.9 g of cyclopentadiene added through the condenser in small portions over a period of 25 minutes. The mixture was then heated on a water bath for 1 hour. Vacuum distillation yielded 12.75 g (85%) of 1-propionyl-2,5-endomethylenecyclohexene-3 with b. p. 77-79° (9 mm). After redistillation, the substance had b. p. 78-79° (10 mm), d_4^{20} 0.9915, n_D^{20} 1.4835.

Found %: C 79.95, 79.91; H 9.46, 9.54. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.39.

Semicarbazone: m. p. 174-174.5° (from ethanol).

Found %: C 63.85, 63.61; H 8.29, 8.51; N 20.38, 20.21. $C_{11}H_{17}ON_2$. Calculated %: C 63.74; H 8.27; N 20.27.

Preparation of 1-propionyl-2,5-endomethylenecyclohexene-3 (VIIb) from 5-chloropentanone-3, potassium acetate and cyclopentadiene. Into a flask fitted with a reflux condenser was placed a solution of 9.8 g of potassium acetate and 12.15 g of 5-chloropentanone-3 in 55 ml of 95% ethanol. Then 9.9 g of cyclopentadiene was

added through the reflux condenser. The precipitation of KCl began immediately and the mixture evolved heat noticeably. After 1 hour, the mixture was heated on a boiling water bath for 2 hours. The usual processing yielded 10.8 g (72%) of (VIIb) with b. p. 76-77° (8 mm) and n_D^{20} 1.4838.

Preparation of 1-acetyl-2,3,4,5-dicyclohexanocyclohexene-3 (VIIIa) from 4-acetoxybutanol-2 and 1,1'-dicyclohexenyl. A mixture of 13.0 g of 4-acetoxybutanol-2, 0.98 g of potassium acetate, 16.2 g of 1,1'-dicyclohexenyl and a small amount of hydroquinone were sealed in an ampoule. The ampoule was heated for 18 hours in boiling n-octane. The ampoule was then opened and the mixture poured into water, neutralized with NaHCO_3 and extracted with ether. The ether solution was dried with CaCl_2 . We obtained 17.2 g (74%) of 1-acetyl-2,3,4,5-dicyclohexanocyclohexene-3 (VIIIa) with b. p. 130-132° (2.5 mm) and m. p. 68-68.5° (from methanol) [15].

Reaction of ethyl vinyl ketone with 1,1'-dicyclohexenyl. A mixture of 8.4 g of ethyl vinyl ketone, 16.2 g of 1,1'-dicyclohexenyl and a small amount of hydroquinone was sealed in an ampoule and the ampoule heated on a water bath for 24 hours. We obtained 15.7 g (64%) of 1-propionyl-2,3,4,5-dicyclohexanocyclohexene-3 (VIIIb) with b. p. 148-150° (3 mm) and m. p. 53-53.5° (from methanol).

Found %: C 82.82, 82.74; H 10.84, 10.70. $\text{C}_{17}\text{H}_{26}\text{O}$. Calculated %: C 82.87; H 10.64.

Preparation of 1-propionyl-2,3,4,5-dicyclohexanocyclohexene-3 (VIIIb) from 5-acetoxypentanone-3 and 1,1'-dicyclohexenyl. A mixture of 14.4 g of 5-acetoxypentanone-3, 0.98 g of potassium acetate, 16.2 g of 1,1'-dicyclohexenyl and a small amount of hydroquinone was heated in a sealed ampoule for 18 hours in boiling n-octane. The usual processing yielded 16.5 g (67%) of substance (VIIIb) with b. p. 154-156° (4 mm) and m. p. 53-53.5° (from methanol).

SUMMARY

1. The action of potassium acetate in acetic acid on 4-chlorobutanone-2 and 5-chloropentanone-3 yielded 4-acetoxybutanone-2 and 5-acetoxypentanone-3, respectively.
2. The action of potassium acetate in ethanol on 4-chlorobutanone-2 and 5-chloropentanone-3 in the presence of cyclopentadiene yielded the products of the addition of cyclopentadiene to methyl vinyl ketone and ethyl vinyl ketone, respectively.
3. Methyl vinyl ketone and ethyl vinyl ketone readily add acetic acid in the presence of potassium acetate.
4. From the results presented above it follows that the reaction of β -chloroketones with potassium acetate in acetic acid, leading to the formation of β -acetoxyketones, proceeds through the intermediate formation of vinyl ketones.
5. The addition of carboxylic acids to methyl vinyl and ethyl vinyl ketones was studied.
6. Heating 4-acetoxybutanone-2 and 5-acetoxypentanone-3 with 1,1'-dicyclohexenyl in the presence of potassium acetate yielded products of the addition of 1,1'-dicyclohexenyl to methyl vinyl and ethyl vinyl ketone, respectively. It was thus shown that β -acetoxyketones split out acetic acid when heated in the presence of potassium acetate.

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THE FIELD OF ORGANIC INSECTOFUNGICIDES

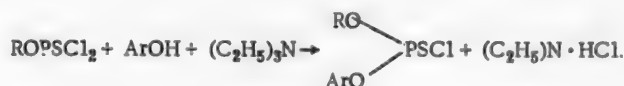
XLV. SYNTHESIS OF ALKYL ARYL CHLOROTHIOPHOSPHATES AND ALKYL ARYL THIOPHOSPHAMIDES

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We recently showed [1] that the interaction of phosphorus thiotrichloride with phenols in the presence of triethylamine gives satisfactory yields of the corresponding aryl dichlorothiophosphates and the interaction of phenols with dialkyl chlorothiophosphates in the presence of this amine forms dialkyl aryl thiophosphates.

It seemed interesting to use the reaction of alkyl dichlorothiophosphates with phenols in the presence of triethylamine for the synthesis of alkyl aryl chlorothiophosphates, which have been studied very little up to the present time, since the discovery of a simple and convenient method of preparing these compounds would make it possible to obtain a large series of new derivatives of thiophosphoric acid with a high insecticidal activity. The first experiments on the reaction of alkyl dichlorothiophosphates on phenols in the presence of triethylamine showed that the corresponding alkyl aryl chlorothiophosphates could be obtained in quite satisfactory yields by this method. This reaction may be represented by the following general scheme:



The compounds we synthesized and their properties are presented in Table 1.

TABLE 1

Properties of O-alkyl O-aryl Chlorothiophosphates $\begin{matrix} \text{RO} \\ \text{ArO} \end{matrix} \text{PSCl}$

Name	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Yield in %	% Cl		% P	
					found	calc.	found	calc.
O-Ethyl O-phenyl chlorothiophosphate *	94—96° (0.5)	1.2499	1.5390	55	14.93, 15.04	15.01	13.02, 13.12	13.17
O-Ethyl O-4-chlorophenyl chlorothiophosphate	113—116 (0.2)	1.3664	1.5520	60	25.81, 25.79	26.18	11.57, 11.80	11.43
O-Ethyl O-2,4-dichlorophenyl chlorothiophosphate	133—137 (0.4)	1.4386	1.5600	58	34.26	34.85	10.16, 10.19	10.14
O-Ethyl O-2,4,5-trichlorophenyl chlorothiophosphate	163—166 (0.7)	1.5548	1.5981	50	41.26	41.78	8.61, 8.63	9.11
O-Ethyl O-4-nitrophenyl chlorothiophosphate *	160 (0.2)	1.4543	1.5740	54	12.42, 12.51	12.61	10.70, 10.62	11.03

* Prepared by both the first and the second methods.

TABLE 2

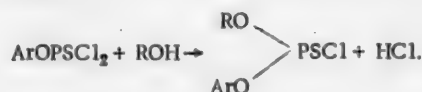
Properties of O-alkyl O-aryl Thiophosphamides

R	Ar	R'	R''	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Yield (in %)	% P		% N		LD ₅₀ for rice cur- culionidae (in %)**
								found	calc.	found	calc.	
CH ₃ C ₂ H ₅	O ₂ NC ₆ H ₄	C ₂ H ₅	C ₂ H ₅	158-164° (0.1), m.p. 34°	1.3086	1.5700	69	10.27	10.73	9.30	9.70	— 0.007
								9.90	9.75	8.62	8.80	
C ₂ H ₅	C ₆ H ₅	CH ₃ H	C ₂ H ₅	153-155 (0.2) 165-170 (0.2) 120-122 (0.4)	1.2468 1.2663 1.1475	1.5460 1.5720 1.5238	52 58 70	10.80	10.70	9.53	9.66	0.008 0.008 Low toxicity
								8.73	9.17	8.06	8.29	
								11.30	11.55	5.07	5.14	

* Did not distill at 0.2 mm. The analysis was carried out after the light fractions had been removed at 0.2 mm.

** LD₅₀ of Thiophos for rice curculionidae is 0.003-0.006%.

Alkyl aryl chlorothiophosphates may also be obtained by the interaction of aryl dichlorophosphates with alcohols by the scheme



This reaction proceeds completely analogously to the reaction of alcohols with alkyl dichlorothiophosphates [2] with the use of a large excess of alcohol. We studied this reaction on the examples of the interaction of phenyl and p-nitrophenyl dichlorothiophosphates with alcohol. The constants of the alkyl aryl chlorothiophosphates obtained were the same as the constants of these compounds which were obtained by the reaction of alkyl dichlorothiophosphates with phenols in the presence of triethylamine.

From the alkyl aryl chlorothiophosphamides synthesized by the above method and various amines we obtained previously undescribed O-alkyl O-aryl thiophosphamides, whose properties are presented in Table 2.

The synthesis of this type of compound is of great interest since the corresponding dialkyl thiophosphamides have quite a strong insecticidal action [3, 4].

The insecticide properties of the compounds we synthesized were studied by P. V. Popov, who showed that all the alkyl 4-nitrophenyl thiophosphamides are active insecticides with a strength approaching that of O,O-diethyl O-4-nitrophenyl thiophosphate. The alkyl aryl thiophosphamides are a new class of organophosphorus insecticides, discovered in our laboratory, and their study is of great interest.

EXPERIMENTAL

1. Interaction of alkyl dichlorothiophosphates with phenols in the presence of triethylamine. Into a flask with a reflux condenser, dropping funnel and mechanical stirrer capable of not less than 300 revolutions per minute, was placed a solution of 0.1 mole of phenol and 0.11 mole of triethylamine in 150 ml of chlorobenzene and at -8 to -10° the alkyl dichlorothiophosphate was added gradually to it. The alkyl dichlorothiophosphate was added over a period of 30-60 minutes and then the reaction mixture was kept at -8° for a further 10 minutes and diluted with water. The chlorobenzene layer was separated, carefully washed with water and dried and the chlorobenzene removed in vacuum. The residue after removal of the chlorobenzene was fractionated in high vacuum. The compounds obtained and their properties are given in Table 1.

2. Interaction of aryl dichlorothiophosphates with alcohols. 0.1 mole of aryl dichlorothiophosphate with 1-4

moles of alcohol was stirred vigorously in a flask with a reflux condenser for 4-10 hours at 20-30°. The reaction mixture was then diluted with water and the oil which formed was separated, washed with water, dried and fractionated in vacuum. The best yields of alkyl aryl chlorothiophosphates were obtained by the interaction of 1 mole of aryl dichlorothiophosphate with 20-30 moles of alcohol. When the reaction was performed in benzene or chlorobenzene, good yields of alkyl aryl chlorothiophosphates were also obtained by the use of 10 moles of alcohol to 1 mole of aryl dichlorothiophosphate. The alkyl aryl chlorothiophosphates obtained by this method are marked with an asterisk in Table 1.

3. Preparation of O-alkyl O-aryl thiophosphamides. With vigorous stirring the appropriate amine was added to a solution of alkyl aryl chlorothiophosphate in benzene or ether (from 1500 to 3500 ml of solvent to 1 mole of alkyl aryl chlorothiophosphate) at 0-20° and the reaction mixture was kept at this temperature for 5-10 hours. The amine salt which separated was then dissolved in water, the amide solution dried, the solvent removed in vacuum and the residue fractionated in high vacuum. The compounds obtained and their properties are given in Table 2. Two moles of amine were used for each mole alkyl aryl chlorothiophosphate. It should be noted that this method yielded O-alkyl O-aryl thiophosphamides in an almost analytically pure state even without fractionation in high vacuum.

SUMMARY

1. Two new methods were developed for the preparation of O-alkyl O-aryl chlorothiophosphates. These methods were used to synthesize a series of previously undescribed compounds, which are given in Table 1.
2. By the interaction of O-alkyl O-aryl chlorothiophosphates with amines we synthesized a series of previously undescribed O-alkyl O-aryl thiophosphamides, many of which were found to be very active insecticides.

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THE FIELD OF ORGANIC INSECTOFUNGICIDES

XLVI. SYNTHESIS OF SOME PHOSPHONOACETIC ACID DERIVATIVES

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One of the main trends in the study of organophosphorus insecticides is the synthesis and investigation of compounds with the general formulas (I) and (II), containing a radical at the phosphorus with quite acid properties [1-5].



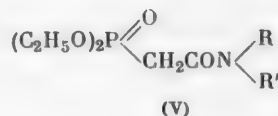
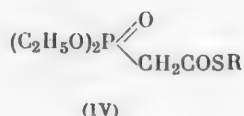
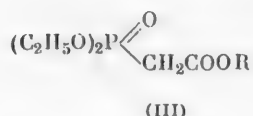
In the opinion of Shrader [1] and some other investigators, this type of phosphorus compound readily phosphorylates enzyme systems important to life in insects and this leads to the death of the latter. The insecticide properties of compounds not containing radicals of an acid character have been studied much less and are largely presented in various patents. Since this problem is of great interest for understanding the mechanism of action of organophosphorus insecticides on insects, we undertook a special investigation of the synthesis of various substances of this type.

Properties of Phosphonoacetic Acid Derivatives

Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Yield (%)	P analysis (%)	
					found	calc.
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{COSC}_2\text{H}_5$	115—120° (0.2)	1.1362	1.4580	45	12.66, 12.12	12.91
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{COOC}_2\text{H}_5$	115—120 (0.18)	1.1456	1.4632	35	11.81, 11.83	11.40
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{COOC}_2\text{H}_4\text{Cl}(4)$	152—154 (0.3)	1.2572	1.4980	50	10.38, 10.23	10.21
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{COSC}_2\text{H}_4\text{Cl}(4)$	143—146 (0.3)	1.2485	1.5231	70	10.00, 10.09	9.61
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{COOC}_2\text{H}_4\text{Cl}_2(2, 4, 5)$	139—141 (0.1)	1.3617	1.5183	45	8.29, 8.65	8.25
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{COSC}_2\text{H}_4\text{Cl}_2(2, 4, 5)$	164—166 (0.2)	1.4131	1.5482	50	8.07, 8.02	7.94
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{CON}(\text{C}_2\text{H}_5)_2$	123—124 (0.1)	1.0988	1.4586	20	11.92, 11.53	12.30
$(\text{C}_2\text{H}_5\text{O})_2\text{P}(=\text{O})\text{CH}_2\text{CONHC}_2\text{H}_5$	174—177 (0.25)	1.1842	1.5245	52	11.41, 11.25	11.44

First of all it seemed interesting to study the insecticide properties of various derivatives of phosphonoacetic acid, since in these compounds the bond of the phosphorus with the acetic acid residue is quite strong and withstands the action of both acids and alkalis [6-10]. As is known, esters of phosphonoacetic acid are readily obtained by the A. E. Arbuzov reaction [6] by the interaction of monochloroacetic esters with a trialkyl phosphite or sodium dialkyl phosphite [7, 8]. Despite the simplicity of the preparation, a very limited number of esters of phosphonoacetic acid have been described up to the present time [6-11]. Even fewer ester amides of phosphonoacetic acid have been described [8, 10], and derivatives of phosphonothioacetic acid have not been described at all. The insecticide properties of these compounds have not been studied either. Only the reaction products of esters and amides of trichloroacetic acid with trialkyl phosphites have been patented for use as insecticides [12-16], but these substances are apparently full esters of phosphoric acid and not of phosphonodichloroacetic acid since the Arbuzov reaction proceeds anomalously with trichloroacetic acid derivatives.

In order to study the insecticide properties and to accumulate material on the relation between insecticide activity and the structure of organophosphorus compounds and on the mechanism of action of these compounds on insects, we undertook the synthesis of compounds with the general formulas (III), (IV) and (V). We synthesized these compounds by the Arbuzov reaction by the interaction of triethyl phosphite with esters of monochloroacetic and monochlorothioacetic acids and amides of monochloroacetic acid. The compounds we synthesized and their properties are given in the Table.



The insecticide properties of the compounds we synthesized were studied by P. V. Popov and N. S. Ukrainets, who showed that the esters of phosphonoacetic acid have a very weak insecticide action, while esters of phosphonothioacetic acid are very active contact and systemic insecticides. The aromatic esters of phosphonothioacetic acid are especially active. Thus, for example, the LD₅₀ of the triethyl ester of phosphonothioacetic acid is 0.003 and that of the diethyl 4-chlorophenyl ester of phosphonothioacetic acid is 0.001%. Amides of phosphonoacetic acid show a comparatively weak activity.

The data presented show conclusively that active insecticides may be found not only among compounds with structures (I) and (II), but also among the other substances and that the interaction of organophosphorus compounds with the enzyme systems of insects may proceed in different directions.

EXPERIMENTAL

The triethyl phosphite required for the reaction was obtained by the method developed recently in our laboratory (from phosphorus trichloride and magnesium ethylate) [17]. Esters of monochlorothioacetic acid were obtained from chloroacetyl chloride and mercaptan in the presence of pyridine.

Triethyl phosphate was condensed with esters of chloroacetic and chlorothioacetic acids and amides of chloroacetic acid under the following conditions: into a flask with a reflux condenser and a mechanical stirrer was placed a mixture of the reagents and when the spontaneous evolution of heat was complete, the mixture was heated for 4-10 hours at 100-130°. In some cases the spontaneous evolution of heat was quite strong and the temperature rose to 140-150°. Thus, for example, when triethyl phosphite was mixed with ethyl monochlorothioacetate, the temperature rose rapidly to 150° and after a mixture of triethyl phosphite had been heated with monochloroacetanilide at 40° for a short time, the temperature rose to 147°.

When the reaction was complete, the light fractions (unreacted products) were distilled from the reaction mixture in vacuum and the residue fractionated in high vacuum. The compounds we obtained and their properties are given in the table.

SUMMARY

1. By the interaction of triethyl phosphite with esters of monochloroacetic and monochlorothioacetic acids and amides of monochloroacetic acid we synthesized a series of previously undescribed derivatives of phosphonoacetic and phosphonothioacetic acids.

Most esters of phosphonothioacetic acid are active insecticides.

2. On the basis of the data obtained, the hypothesis was put forward that the mechanism of the phosphorylating action of organophosphorus compounds on enzyme systems of insects has different forms.

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THE FIELD OF ORGANIC INSECTOFUNGICIDES

XLVII. INTERACTION OF ARYLDIAZONIUM SALTS WITH DIALKYL DITHIOPHOSPHATES

N. N. Mel'nikov, A. F. Grapov, and K. D. Shvetsova-Shilovskaya

We recently showed that the interaction of aryldiazonium salts with dialkyl dithiophosphates [1] and dialkyl thiophosphates [2] formed, as the main reaction products, the corresponding mixed esters of dithiophosphoric and thiophosphoric acids. Since this reaction is a good new method of preparing mixed esters of thiophosphoric acids, it seemed interesting to study it on a larger number of examples, all the more so as such mixed esters have a high insecticide activity.

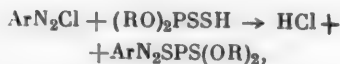
By the interaction of various aryldiazonium salts with dialkyl dithiophosphates under the conditions we described previously, we synthesized a series of new mixed esters of dithiophosphoric acid, whose properties are given in Table 1.

TABLE 1

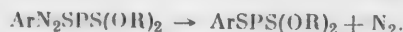
Properties of Mixed Esters of Dithiophosphoric Acid.

Formula	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Found (%)			Calc. (%)		
					C	H	P	C	H	P
$(CH_3O)_2PS_2C_6H_4Cl$	25	115.5—116 (0.15)	1.3235	1.5948	—	—	11.82, 11.96	—	—	11.93
$(C_2H_5O)_2PS_2C_6H_4OCH_3$ -(4)	28	129.5—130 (0.15)	1.2303	1.5680	45.30	5.84	10.58	45.15	5.71	10.87
$(C_2H_5O)_2PS_2C_6H_4COOCH_3$ -(2)	33	144—145 (0.2)	1.2330	1.5648	45.50, 45.84	5.72, 5.75	9.71, 9.72	44.99	5.32	9.67
$(iso-C_3H_7O)_2PS_2C_6H_5$	65	102.5—104 (0.08)	1.1174	1.5487	—	—	11.21, 11.31	—	—	10.66
$(iso-C_3H_7O)_2PS_2C_6H_4Cl$ -(4)	38	121.5—123.5 (0.12)	1.1904	1.5612	—	10.56, 10.91	—	—	10.50 (Cl)	—
$(iso-C_3H_7O)_2PS_2C_6H_4OCH_3$ -(4)	32	125—127 (0.1)	1.1367	1.5451	48.28, 48.29	7.10, 7.18	9.28, 9.38	48.73	6.55	9.66
$(n-C_3H_7O)_2PS_2C_6H_5$	48	125.5—127.5 (0.28)	1.1262	1.5487	49.39, 49.46	7.10, 7.12	10.33, 10.51	49.63	6.60	10.66

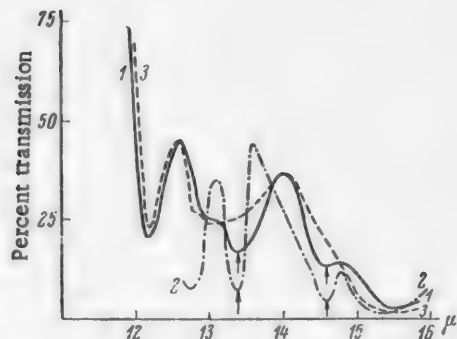
The reaction of aryldiazonium salts with dialkyl dithiophosphoric acids and their salts [1] apparently proceeds by a homolytic mechanism, which may be confirmed by the fact that the corresponding dialkyl aryldiazonium dithiophosphate is formed as an intermediate product



and on decomposition, this gives an O,O-dialkyl aryl dithiophosphate and nitrogen



We were able to isolate such an intermediate product in the interaction of p-chlorophenyldiazonium chloride with diisopropyl dithiophosphoric acid. Diisopropyl p-chlorophenyldiazonium dithiophosphate is a yellow crystalline substance which dissolves readily in alcohol, acetone, ether and isooctane and has m. p. 33-35°. It rapidly decomposes in air. When decomposed in an aqueous medium in the presence of cuprous salts, it gives a satisfactory yield of O,O-diisopropyl S-p-chlorophenyl dithiophosphate.



Infrared absorption spectra. 1) Reaction product of potassium di-sec-butyl dithiophosphate with phenyldiazonium chloride, 2) tetra-sec-butyl thiophosphonyl disulfide, 3) O,O-diisopropyl S-phenyl dithiophosphate.

action of phenyldiazonium chloride with di-sec-butyl dithiophosphate yields a mixture of disulfide and O,O-di-sec-butyl S-phenyl dithiophosphate, as was established from infrared spectra, since this mixture could not be fractionated in high vacuum. O,O-Di-sec-butyl S-phenyl dithiophosphate predominates in this mixture, as can be seen from a comparison of the IR-absorption spectra (figure).^{*} An analogous mixture was also obtained by the interaction of aryldiazonium salts with dipropyl dithiophosphates.

The yields of products from the reaction of potassium diisopropyl dithiophosphate with aryldiazonium salts in acid and neutral media are presented in Table 2.

TABLE 2

Products from the Reaction of Potassium Diisopropyl Dithiophosphate with Aryldiazonium Salts

Aryldiazonium salt	Medium	Formula of reaction product	Yield (in%)
$\text{C}_6\text{H}_5\text{N}_2\text{Cl}$	Neutral	$(\text{iso-C}_3\text{H}_7\text{O})_2\text{PS}_2\text{C}_6\text{H}_5$	65
	Acid	$[(\text{iso-C}_3\text{H}_7\text{O})_2\text{PSS}]_2$	98
$\text{p-ClC}_6\text{H}_4\text{N}_2\text{Cl}$	Neutral	$(\text{iso-C}_3\text{H}_7\text{O})_2\text{PS}_2\text{C}_6\text{H}_4\text{Cl}$	35
	Acid	$[(\text{iso-C}_3\text{H}_7\text{O})_2\text{PSS}]_2$	74
$\text{p-CH}_3\text{OC}_6\text{H}_4\text{N}_2\text{Cl}$	Neutral	$(\text{iso-C}_3\text{H}_7\text{O})_2\text{PS}_2\text{C}_6\text{H}_4\text{OCH}_3$	32
	Acid	$[(\text{iso-C}_3\text{H}_7\text{O})_2\text{PSS}]_2$	75, 35
$\text{p-O}_2\text{NC}_6\text{H}_4\text{N}_2\text{Cl}$	The same	$[(\text{iso-C}_3\text{H}_7\text{O})_2\text{PSS}]_2$, $\text{ClC}_6\text{H}_4\text{NO}_2$	15, insignificant

* The absorption spectra were plotted by L. Z. Osityanskaya, to whom we are grateful.

EXPERIMENTAL

We prepared most of the mixed esters of dithiophosphoric acid, presented in Table 1, under the conditions described in the previous communication [1]. The synthesis of only those compounds whose preparation conditions differed from those described previously are given below.

1. O,O-Dimethyl S-p-chlorophenyl dithiophosphate. 13.0 g of p-chloroaniline was dissolved in 50 ml of concentrated hydrochloric acid and 1500 ml of water and diazotized with 8 g of sodium nitrite. To the solution of diazo compound obtained was added 15.8 g of dimethyl dithiophosphoric acid, 1 g of cuprous chloride and the solution slowly heated to 50°. When the evolution of nitrogen had ceased, the reaction mixture was extracted with ether and after the extract had been dried, the ether was removed. The residue was fractionated in vacuum. Fractionation yielded the two following fractions: 1st 45-60° at 0.2-0.3 mm, 2.6 g - original dimethyl dithiophosphoric acid and 2nd, 120-135° at 0.3-0.6 mm, 7.3 g, which gave a precipitate from alcohol and acetone on cooling. The substance had m. p. 187-187.5°.

Found %: N 11.5, 10.95. $C_{12}H_8N_2Cl_2$. Calculated %: N 11.1

Literature data: 4,4'-dichloroazobenzene melts at 188°.

After removal of the 4,4'-dichloroazobenzene, the filtrate was distilled twice in vacuum. The O,O-dimethyl S-p-chlorophenyl dithiophosphate obtained thus had b. p. 115.5-116° at 0.15 mm, d_4^{20} 1.3235, n_D^{20} 1.5948.

2. Tetraisopropyl thiophosphonyl disulfide. 6.15 g of p-anisidine was dissolved in 50 ml of concentrated hydrochloric acid and 30 ml of water and diazotized in the usual way with 3.5 g of sodium nitrite in 20 ml of water. To the diazo solution obtained were added 12.6 g of potassium diisopropyl dithiophosphate in 50 ml of water and 1 g of cuprous chloride. When the evolution of gas was complete, the reaction mixture was heated to 40° and then cooled to 0° and the crystals which separated were collected by filtration (8 g). After recrystallization from alcohol, the substance had m. p. 90-91°. A mixture with pure tetraisopropyl thiophosphonyl disulfide melted at 90-91° and did not show depression.

After removal of the disulfide, the filtrate was steam distilled to give an oil, which was extracted with chloroform and then vacuum distilled after removal of the solvent. The b. p. was 70-72° at 40 mm and the yield 1.9 g. The picrate had m. p. 81-82°. A mixed melting point of this picrate with that of anisole was not depressed.

Potassium diisopropyl dithiophosphate was reacted with other aryldiazonium salts in an acid medium under completely analogous conditions and likewise for the reaction of potassium di-sec-butyl dithiophosphate with phenyldiazonium chloride.

3. O,O-Diisopropyl S-phenyl dithiophosphate. A solution of 3.22 g of aniline hydrochloride in 25 ml of alcohol was diazotized with 3 g of isoamyl nitrite in the presence of 0.1 g of hydrochloric acid at 0-2°. To the solution was added 50 ml of ether and the precipitated phenyldiazonium chloride was collected by filtration, washed twice with ether (20 ml portions) and dissolved in 50 ml of water. To the aqueous solution of phenyldiazonium chloride were added 6 g of potassium diisopropyl dithiophosphate in 35 ml of water and 0.5 g of cuprous chloride. The usual processing yielded 4.5 g of an oil with b. p. 102.5-104° at 0.08 mm, d_4^{20} 1.1174, n_D^{20} 1.5487.

4. O,O-Diisopropyl S-p-chlorophenyl dithiophosphate. To the diazo solution obtained from 5 g of p-chloroaniline hydrochloride and 6 g of isoamyl nitrite was added a solution of 10.1 g of potassium diisopropyl dithiophosphate in 75 ml of water. On cooling, the mixture deposited crystals with m. p. 33-35°, which evolved nitrogen when heated in an aqueous medium with cuprous chloride and gave O,O-diisopropyl S-p-chlorophenyl dithiophosphate. This could also be prepared without isolation of the intermediate compound.

In the latter case, cuprous chloride was added after the solution of the diazonium salt had been mixed with the dithiophosphate and the reaction mixture was slowly heated to 20-30°. When the evolution of nitrogen ceased, the reaction product was isolated in the usual way. The properties of the compounds obtained by this method are presented in Table 1.

5. Tetra-sec-butyl thiophosphonyl disulfide. To 5.6 g of potassium di-sec-butyl dithiophosphate in 25 ml of water was added 2.6 g of iodine in 50 ml of a 20% aqueous solution of potassium iodide. The oil which separated was extracted with ether and the ether solution washed with water and dried with potassium carbonate. Removal of the ether in vacuum yielded an oil.

d_4^{20} 1.1267, n_D^{20} 1.5272.

Found %: C 39.76, 39.67; H 8.00, 7.99; P 12.04, 12.21. $C_{16}H_{16}O_4P_2S_4$. Calculated %: C 39.82; H 7.52; P 12.83.

SUMMARY

The interaction of dialkyl dithiophosphates and dialkyl dithiophosphoric acids with aryldiazonium salts was studied. It was shown that in the case of potassium diisopropyl dithiophosphate, the reaction may proceed in two directions: in a neutral medium to form mixed esters of dithiophosphoric acid and in an acid medium to give predominantly disulfides. Other dialkyl dithiophosphates react with aryldiazonium salts to form predominantly mixed esters of dithiophosphoric acid. Hardly any of the compounds synthesized have been described in the literature.

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RADICAL AND IONIC ALKYLATION OF THE AROMATIC NUCLEUS

VIII. A CONTRIBUTION ON TRICHLOROMETHYLATION OF NAPHTHALENE

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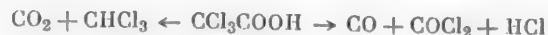
It is not possible to obtain trichloromethyl derivatives by condensations of carbon tetrachloride with aromatic compounds in the presence of AlCl_3 . These reactions give diaryldichloromethanes and triarylchloromethanes [1].

There are a few communications on the radical trichloromethylation of the aromatic nucleus [2-10]. The thermal decomposition of benzoyl and naphthoyl peroxides in CCl_4 solution and the subsequent isolation of hexachloroethane and trichloromethyl aromatic compounds have been described in the literature [2-5]. The trichloromethylation of benzene and naphthalene was observed during the thermal decomposition of arylmercury compounds in CCl_4 . Nesmeyanov and his co-workers [10] described the trichloromethylation of naphthalene (xylene and phenanthrene) with trichloroacetic acid in the presence of cupric salts. The authors considered that the decarboxylation of trichloroacetic acid forms the anion CCl_3^- , which then changes into a CCl_3 radical and the latter alkylates naphthalene. In most of this work the trichloromethyl aromatic compounds were not isolated and their yields were determined by the acids formed after alkaline hydrolysis of the reaction mixture.

We undertook to determine the possibility of trichloromethylating naphthalene with carbon tetrachloride in the presence of copper, considering the ease of the homolytic cleavage of CCl_4 under the action of metals [11]. A solution of naphthalene in CCl_4 was heated ($180-200^\circ$, 10-20 hours) with a small amount of copper bronze and after alkaline hydrolysis of the reaction mixture, we obtained α -naphthoic acid. The yields of the hypothetical trichloromethylnaphthalene did not exceed 12% when the experiments were carried out in sealed tubes. Better yields (up to 33%) were obtained in autoclaves with the reaction mixture in contact with the walls of the autoclave. Experiments in sealed tubes with the addition of iron salts (FeCl_3 , FeBr_2 and FeCl_2) showed that the latter had a positive effect. However, we were unable to establish a clear dependence of the α -naphthoic acid yields on the conditions of these reactions. We did not detect hexachloroethane or chloronaphthalene in the condensation products. This compelled us to attempt to isolate trichloromethylnaphthalene in a pure state and compare it with the product formed by Nesmeyanov's method [10].

The reaction of naphthalene with trichloroacetic acid in the presence of cupric chloride and small amounts of pyridine gave up to 31% of α -naphthoic acid. On investigating the composition of the gases liberated during this reaction, it was found that besides hydrogen chloride and carbon dioxide, carbon monoxide (30-70%) and a little phosgene were always detected. This agrees with literature data on the thermal decomposition of trichloroacetic acid in the presence of metals and metal salts [12].

In several experiments it was established that the volume of carbon dioxide liberated was a factor of 2 less than what would be expected according to the yield of α -naphthoic acid. Appreciable amounts (up to 25%) of chloroform were detected in the fractionation of the reaction mixture. All this gives grounds for considering that trichloroacetic acid probably decomposes in two directions in this reaction.



The condensation of naphthalene with phosgene forms α -naphthoyl chloride, which gives α -naphthoic acid on hydrolysis.



The carboxylation of anthracene and naphthalene by phosgene, formed when mixtures of these hydrocarbons are heated with oxalyl chloride (160-170°), has been described in the literature [13].

Further study of the composition of the reaction products of naphthalene and trichloroacetic acid gave direct confirmation of the scheme presented. It was found that α -naphthoic acid was liberated by simply washing a benzene solution of the reaction mixture with sodium carbonate, without preliminary alkaline hydrolysis. Vacuum fractionation of the reaction mixture gave α -naphthoyl chloride and α -naphthoic acid. Distillation of the products from the condensation of naphthalene with carbon tetrachloride in the presence of copper and iron salts also gave α -naphthoyl chloride. The formation of phosgene from CCl_4 under the action of metals or salts at 180-200° proceeds readily in the presence of water [14]. In our experiments, the small but very variable yields of α -naphthoic acid are explained by the variable moisture content of the reaction mixture. Control experiments (in sealed tubes) with carefully purified and dried reagents (under the action of copper and ferrous bromide) did not give α -naphthoic acid at all or gave very small yields of it.

Thus, the reaction of carbon tetrachloride with naphthalene in the presence of copper at 200° should not be considered as trichloromethylation. The α -naphthoic acid obtained is the product of carboxylation of naphthalene by phosgene. A similar conclusion should be drawn on the reaction of trichloroacetic acid with naphthalene in the presence of cupric chloride. Trichloromethylation does not occur in this case either but the naphthalene is carboxylated by phosgene.

The results we obtained also make it imperative to examine other previously described cases of trichloromethylation of the aromatic nucleus, based on the fact that acids were obtained when the mixture of reaction products was hydrolyzed.

TABLE 1

Expt. No.	Substances added to copper (in g)	Naphthalene recovered (in %)	α -Naphthoic acid yield (in %)	Tar (in g)
1	—	75	3	0.6
2	FeCl_3 0.8	67	5	0.8
3	FeBr_2 1.0	42	12	1.8
4	FeCl_2 0.6	48	11	1.4
5	—	24	33	1.2
6	—	12	24	5.2
7	—	25	30	1.5
8	Without catalyst	32	13	1.8

Note: Molar ratios $\text{CCl}_4 : \text{C}_{10}\text{H}_8 : \text{Cu} = 10 : 1 : 0.1$, naphthalene 4-5 g, temperature 190-200°; heating time 20 hours. Experiments 1-4 were in sealed tubes and 5-8 were in an autoclave.

EXPERIMENTAL

1. Reaction of naphthalene with carbon tetrachloride. The reagents used were CCl_4 , dried calcium chloride, sublimed naphthalene, copper bronze powder and anhydrous iron salts (FeCl_3 , FeBr_2 and FeCl_2). The experiments were performed in refractory sealed tubes heated in a Carius furnace, or in small autoclaves of acid-resistant steel. The cooled reaction mixture was transferred to a flask, treated with excess of 2 N solution of alkali and

steam distilled for 1 hour. The solution remaining in the distillation flask was filtered and acidified with hydrochloric acid; this precipitated α -naphthoic acid with m. p. 159° (from 30% alcohol). A mixture with an authentic sample of α -naphthoic acid melted at 159°.

Table 1 shows the results of some experiments.

Isolation of α -naphthoyl chloride. 5.3 g of naphthalene, 120 ml of carbon tetrachloride, 0.4 g of copper bronze and 2 g of FeBr_3 were heated in sealed tubes for 12 hours at 180-200°. When the cooled tubes were opened,

TABLE 2

Experiment No.	Temperature	Reaction time (in hours)	Gaseous products			α -Naphthoic acid (in %)		
			total (in liters)	composition of gas (in vol. %)		isolation method		
				CO	CO ₂	1	2	3
1	180-190°	0.5	1.65	28	70	16.3	—	—
2	190-195	2	2.5	75	25	30.8	—	—
3	155-175	2	0.5	69	29	—	16.7	—
4	175-180	2	1.4	39	58	—	25.5	—
5	155-175	1.5	1.3	47	53	—	26.8	—
6	155-170	2	0.5	72	24	—	14.1	—
7	175-190	1	2.5	39	59	—	—	13.6

Footnote. Molar ratios $\text{CCl}_3\text{COOH} : \text{C}_{10}\text{H}_8 : \text{CuCl}_2 = 1 : 1.5 : 0.1$, pyridine 0.02 g and naphthalene 30 g.

It was found that their contents were under high pressure. The reaction mixture was fractionated. We obtained 2.3 g of naphthalene and 0.7 g (17%) of α -naphthoyl chloride.

B. p. 166° (11 mm), d_4^{20} 1.2694, n_D^{20} 1.6528 [15].

Found %: Cl 17.10. $\text{C}_{11}\text{H}_7\text{OCl}$. Calculated %: Cl 17.16.

Shaking with a concentrated aqueous solution of ammonia yielded α -naphthoamide with m. p. 201°.

Control experiment with dry reagents. Carbon tetrachloride was purified by repeated shaking with an aqueous alcohol solution of potassium hydroxide. The solvent was then dried over P_2O_5 and distilled in the absence of air. A fraction with b. p. 75° (730 mm) was dried over phosphorus pentoxide for 24 hours. The naphthalene was dried in a desiccator over CaCl_2 for 2 days. The experiment was carried out under the same conditions as those described above. The reaction mixture was steam distilled. The small residue in the flask was hydrolyzed with 15 ml of 10% NaOH (heating for 4 hours). No α -naphthoic acid was liberated when the alkaline solution was acidified. About 0.1 g of α -naphthoic acid was found in the carbon tetrachloride distilled in steam (by shaking with alkali solution and acidification of the extract). An attempt to isolate hexachloroethane gave no results.

2. Reaction of naphthalene with trichloroacetic acid [10]. The experiments were performed in a three-necked flask attached to a reflux condenser. The mixture of reagents was heated for 1-2 hours at 155-190° (thermometer in liquid). The gaseous products passed through the condenser and were collected over dilute acid. The gases were analyzed quantitatively in an Orsat apparatus.

The reaction products were isolated by the three following methods: 1) alkaline hydrolysis of the reaction mixture as described above; the first steam distillates contained chloroform and the amount of this was estimated; 2) the reaction mixture was extracted with benzene, the benzene solution shaken several times with 5% sodium carbonate and the sodium carbonate solution acidified to liberate α -naphthoic acid; a further small amount of the latter was obtained by alkaline hydrolysis of the residual benzene solution; 3) a benzene solution of the reaction mixture was filtered, dried and fractionated in vacuum after removal of the benzene; fractions of α -naphthoic acid and α -naphthoyl chloride were isolated.

The results of some experiments are given in Table 2.

The α -naphthoic acid isolated had m. p. 159°. According to constants, analysis and reactions, the α -naphthoyl chloride was identical with that described above. Phosgene was detected by the formation of ethyl chlorocarbonate with anhydrous alcohol and the preparation of diphenylurea with m. p. 189°.

SUMMARY

1. The interaction of naphthalene with carbon tetrachloride in the presence of copper bronze and iron salts at 200° formed α -naphthoyl chloride (up to 30%). The reaction proceeded through phosgene due to traces of moisture in the mixture. No trichloromethylation of naphthalene occurred under the given conditions.

2. Apparently, there is no trichloromethylation either in the reactions of naphthalene with trichloroacetic acid in the presence of cupric chloride. Trichloroacetic acid is decomposed under the reaction conditions to liberate carbon monoxide, phosgene, hydrogen chloride, carbon dioxide and chloroform. The main products of this reaction are α -naphthoyl chloride and α -naphthoic acid.

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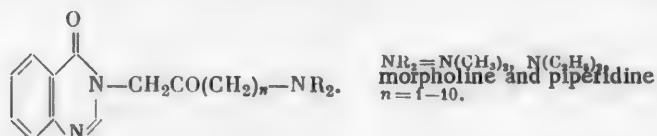
AMINO KETONES OF THE 4-QUINAZOLONE SERIES AS ANALOGS OF FEBRIFUGINE

II. DERIVATIVES OF METHYL ALKYL KETONES

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In a previous communication [1] we described a general method for preparing amino ketones of the type



However, in the case when $n = 2$, due to the weakness of the bond of the substituents with the carbon atom β to the keto group, difficulties were encountered and compounds of this type could not be obtained. With the derivative of methyl propyl ketone and the homologs following it, the aminoalkyl 4-quinazolinyl-3-methyl ketones obtained were stable. They could be obtained by condensation of a halomethyl haloalkyl ketone with 4-quinazolinone and subsequent condensation of the haloalkyl 4-quinazolinyl-3-methyl ketone formed with the desired amine or by first synthesizing the halomethyl aminoalkyl ketone and then condensing it with 4-quinazolinone. We preferred the first variant since it made it possible to obtain a series of amino ketones from the same intermediate product (halomethyl haloalkyl ketone); in addition, halomethyl amino ketones can undergo intramolecular cyclization giving a quaternary ammonium salt.

To synthesize amino ketones where $n = 3$, it was necessary to prepare bromomethyl γ -chloropropyl ketone. This was synthesized by preparing acetopropyl chloride and brominating it with dioxane dibromide [2]. The end of the bromination was determined by the decolorization of the dioxane dibromide. Condensation of the chloro bromo ketone with 4-chloroquinazolinone with the participation of an equivalent amount of sodium ethylate in alcohol gave a good yield of 3- γ -chloropropyl-4-quinazolinone,* which was reacted in a benzene medium with diethylamine, piperidine and morpholine to synthesize γ -diethylaminopropyl, γ -N-piperidinopropyl and γ -N-morpholinopropyl 4-quinazolinyl-3-methyl ketone, respectively. The reactions with morpholine and piperidine occurred in boiling benzene and that with diethylamine occurred in a sealed tube at 130-140° in the presence of KI.

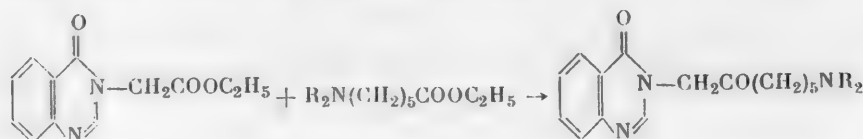
In a biological study, the compounds obtained showed a very weak antimalarial activity.

Derivatives of methyl butyl ketone were obtained by the same scheme. The bromomethyl 4-bromobutyl ketone required for these syntheses was obtained from acetoacetic ester and 1,3-chlorobromopropane through the ethyl ester of 2-methyldihydropyran-3-carboxylic acid, which was isolated but treated directly with

* This is a direct translation of the Russian which appears to be incorrect. It probably should read as follows: Condensation of the chloro bromo ketone with 4-quinazolinone with the participation of an equivalent amount of sodium ethylate in alcohol gave a good yield of γ -chloropropyl 4-quinazolinyl-3-methyl ketone —Publisher's note.

concentrated hydrobromic acid to give methyl 4-bromobutyl ketone [3] (acetobutyl bromide); the latter was then treated with dioxane dibromide in methanol. Bromomethyl δ -bromobutyl ketone was a very unstable, oily substance and therefore, directly after its preparation it was condensed with 4-quinazalone to form δ -bromobutyl 4-quinazolonyl-3-methyl ketone. So as to exclude any doubts on the structure of this ketone, it was also synthesized by another method from 5-bromoaleryl chloride [4] through diazomethyl bromobutyl ketone, which was treated with HBr at 0° to give pure bromomethyl δ -bromobutyl ketone as a crystalline substance. The latter was found to be considerably more stable than the previous oily dibromo ketone. However, its condensation with 4-quinazalone yielded the same δ -bromobutyl 4-quinazolonyl-3-methyl ketone; a mixed melting point of the two ketones was not depressed. Consequently, in the first case the bromomethyl δ -bromobutyl ketone contained some impurities which changed its properties and which may have been the products of more extensive bromination. Analogs of febrifugine were then obtained by condensation of δ -bromobutyl 4-quinazolonyl-3-methyl ketone with diethylamine, morpholine and piperidine as with the methyl propyl ketone derivative. Of the three preparations obtained, the dihydrochloride of δ -N-morpholinobutyl 4-quinazolonyl-3-methyl ketone was active when tested against avian malaria, while the piperidine analog showed weak activity.

It was proposed to synthesize febrifugine analogs derived from methyl n -amyl ketone by the Claisen reaction from ethyl 4-quinazalone-3-acetate and ϵ -aminocaproic esters.



For this purpose, ethyl 6-bromocaproate [5] was condensed with piperidine, morpholine and diethylamine in benzene. Experiments on the condensation of the amino esters obtained with ethyl 4-quinazalone-3-acetate did not give positive results: As a result of the reaction in both alcohol and benzene, 4-quinazalone-3-acetic acid was recovered. Therefore, these compounds were obtained by the previously tested variant through bromomethyl ϵ -bromoamyl ketone, which was synthesized by treating 6-bromocaproyl chloride with diazomethane and decomposing the diazomethyl 5-bromoamyl ketone with HBr. ϵ -Bromoamyl 4-quinazolonyl-3-methyl ketone was then obtained by the scheme described and used to prepare ϵ -diethylamino-, ϵ -N-piperidino- and ϵ -N-morpholinoamyl 4-quinazolonyl-3-methyl ketones. When these were tested for antimalarial activity on a strain of avian malaria, only the piperidino preparation showed considerable activity.

In addition to the preparations described above, it seemed interesting to synthesize substances with a considerably longer ketone chain since, in analogy with quinoline antimalarial compounds [6], such a lengthening of the chain could substantially influence the biological properties of the compounds. For this purpose we synthesized κ -N-piperidino-, κ -N-morpholino- and κ -N,N-diethylaminodecyl 4-quinazolonyl-3-methyl ketones, starting from undecylenic acid, which was saturated with HBr in the presence of benzoyl peroxide to give an 84.2% yield of pure 11-bromoundecanoic acid with m. p. 49-50° (cf. [7]). In this case the purity of the undecylenic acid we used (m. p. 24.5°) was of considerable importance. The 11-bromoundecanoic acid was converted into its acid chloride, which was then converted into bromomethyl κ -bromodecyl ketone by diazo synthesis in analogy with the previous dibromo ketones. This dibromo ketone was condensed with 4-quinazalone and the κ -bromodecyl 4-quinazolonyl-3-methyl ketone obtained was reacted with diethylamine, piperidine and morpholine. Of the κ -N,N-diethylaminodecyl, κ -N-piperidinodecyl and κ -N-morpholinodecyl 4-quinazolonyl-3-methyl ketones obtained, only the latter showed a weak antimalarial activity.

EXPERIMENTAL

Bromomethyl γ -chloropropyl ketone. In a three-necked flask with a stirrer and thermometer, 20 g of acetopropyl chloride was dissolved in 50 ml of methanol and 39.6 g of dioxane dibromide in 120 ml of methanol added dropwise. The mixture was slowly heated to 52° on a water bath and then after a short time the temperature of the mixture rose spontaneously to 62° and the reaction mixture was decolorized. After being stirred for half an hour at room temperature, the mixture was diluted with 250 ml of water. The oily substance liberated was separated, dried and distilled at 98-102° (8-9 mm) or 112-116° (13 mm) [8]. The yield was 26.4 g (83%). The preparation rapidly acquired a dark orange color in air and light and had a lachrymatory action.

γ -Chloropropyl 4-quinazolonyl-3-methyl ketone (I). In a three-necked flask with a stirrer, reflux condenser and thermometer, 14.6 g of 4-quinazalone was added to a solution of sodium ethylate, prepared from 2.3 g of sodium and 90 ml of anhydrous alcohol, and then 20.8 g of bromomethyl 3-chloropropyl ketone was added in one portion with vigorous stirring. After a short time, the precipitation of NaBr began, the temperature rose to 48° and the alkaline reaction to phenolphthalein disappeared. The mixture was stirred for a further half hour and left overnight. Then 300 ml of water was added and the mixture extracted three times with 200 ml portions of chloroform; the chloroform layer was separated, washed with water and dried. Removal of the chloroform yielded 15.5 g (58.4%) of γ -chloropropyl 4-quinazolonyl-3-methyl ketone with m.p. 150–150.5° (from aqueous alcohol). The product was soluble in chloroform, dioxane, hot benzene and acetone.

Found %: N 10.41. Cl 13.49. $C_{13}H_{13}O_2N_2Cl$. Calculated %: N 10.58; Cl 13.30.

The oxime was prepared by heating 0.3 g of ketone, 0.34 g of $NH_2OH \cdot HCl$ and 0.5 g of CH_3COOK in 10 ml of water on a water bath for 6 hours. The yield was 0.18 g and the m. p. 165–166°.

Found %: N 14.83. $C_{13}H_{14}O_2N_2$. Calculated %: N 15.03.

Dihydrochloride of γ -N-piperidinopropyl 4-quinazolonyl-3-methyl ketone (II). In a three-necked flask with a stirrer, reflux condenser and thermometer, 3.4 g of piperidine was added to a solution of 3.4 g of ketone (I) heated to 54° and the mixture was boiled and stirred for 10.5 hours. During the boiling, crystals of piperidine hydrochloride precipitated and the solution acquired a dark red color. After the heating, the piperidine hydrochloride (1.2 g, m. p. 231–235.5°) was removed, 10 ml of water added to the filtrate, the benzene layer separated from the aqueous one and dried and the benzene removed in vacuum; the residue was dissolved in 3 ml of anhydrous alcohol and made acid to Congo Red by the addition of a solution of HCl in anhydrous alcohol. Cooling yielded 1.9 g (50%) of the dihydrochloride of 3-N-piperidinopropyl 4-quinazolonyl-3-methyl ketone with m. p. 213–214° (from anhydrous alcohol).

Found %: N 10.56; Cl 18.34. $C_{18}H_{23}O_2N_3 \cdot 2HCl$. Calculated %: N 10.87; Cl 18.35.

The oxime was obtained analogously to the previous oxime. 0.2 g of the dihydrochloride yielded 0.14 g of oxime as needles with m. p. 154–155°.

Found %: N 16.77. $C_{18}H_{24}O_2N_4$. Calculated %: N 17.05.

The dihydrochloride of γ -N-morpholinopropyl 4-quinazolonyl-3-methyl ketone was obtained analogously to the previous compound with the difference that the reaction mixture was boiled for 24 hours and the residue after removal of the benzene was dissolved in acetone. The yield was 49.2% and the m. p. 202–203° (from alcohol).

Found %: N 10.64, 10.31; Cl 17.28, 17.30. $C_{17}H_{21}O_3N_3 \cdot 2HCl$. Calculated %: N 10.74; Cl 17.22.

γ -Diethylaminopropyl 4-quinazolonyl-3-methyl ketone (III). A mixture of 1 g of ketone (I), 0.58 g of diethylamine, 0.2 g of KI and 40 ml of benzene was heated in a sealed tube at 130–140° for 8 hours. After the heating, the diethylamine hydrochloride (m. p. 219–221°) was removed and the benzene solution washed with water. Removal of the benzene yielded a yellow, crystalline residue, which was washed carefully with water and dried. We obtained 0.51 g (46.3%) of product with m. p. 94–95°. It was soluble in benzene, chloroform and anhydrous alcohol.

Found %: N 13.64. $C_{17}H_{23}O_2N_3$. Calculated %: N 13.94.

Bromomethyl δ -bromobutyl ketone. a) In a bromination similar to that of acetopropyl chloride described above, 41.4 g of acetobutyl bromide and 57 g of dioxane dibromide yielded 63.8 g of unpurified bromomethyl δ -bromobutyl ketone, which gave 51 g (86%) of product when distilled at 8 mm and 128–140°. The substance had a lachrymatory action and rapidly darkened.

b) Into a three-necked flask with a stirrer, thermometer and dropping funnel, thoroughly cooled in an ice-salt mixture, was placed 9.35 g of diazomethane in 400 ml of absolute ether, which was cooled to –5°, and over a period of 1.5 hours, a solution of 22 g of 5-bromovaleryl chloride in 50 ml of ether was introduced dropwise while the temperature was kept at –5° to –2°. After the solution had been kept at –3 to –1° for 2 hours, dry HBr was passed into it to saturation; 50 ml of water was then added, the ether layer separated, washed with $NaHCO_3$

solution and dried and the ether removed. We obtained 20.7 g (73.2%) of bromomethyl δ -bromobutyl ketone, which completely crystallized on cooling and had m. p. 54-55°.

Found %: Br 61.23. $C_6H_{10}OBr_2$. Calculated %: Br 61.97.

δ -Bromobutyl 4-quinazolonyl-3-methyl ketone (IV) was obtained similarly to ketone (I) from bromomethyl δ -bromobutyl ketone and 4-quinazolone. The yield was 61% and the m. p. 132-133° (from alcohol). The oxime of δ -bromobutyl 4-quinazolonyl-3-methyl ketone, obtained by heating appropriate reagents in an aqueous medium on a water bath for 2.5 hours, had m. p. 156-157° (from chloroform).

Found %: N 12.53, 12.78. $C_{14}H_{16}O_2N_3Br$. Calculated %: N 12.42.

The dihydrochloride of δ -N-piperidinobutyl 4-quinazolonyl-3-methyl ketone was obtained analogously to the previous compound. The pale yellow crystalline powder had m. p. 190-191°. The yield was 58%.

Found %: N 10.05; Cl 17.66. $C_{19}H_{25}O_2N_3 \cdot 2HCl$. Calculated %: N 10.49; Cl 17.70.

The dihydrochloride of δ -N-morpholinobutyl 4-quinazolonyl-3-methyl ketone was obtained analogously. The yield was 65%. The m. p. was 166-167°.

Found %: N 10.01; Cl 16.48. $C_{18}H_{23}O_3N_3 \cdot 2HCl \cdot H_2O$. Calculated %: N 10.00; Cl 16.86.

δ -Diethylaminobutyl 4-quinazolonyl-3-methyl ketone was obtained analogously to ketones (III) by heating diethylamine, ketone (IV) and KI in a sealed tube at 120° for 8 hours. The fine, slightly yellowish crystals had m. p. 104-105. The yield was 61.3%. The product was soluble in benzene and chloroform and insoluble in water.

Found %: N 13.26. $C_{18}H_{25}O_2N_3$. Calculated %: N 13.32.

Ethyl 6-diethylaminocaproate. 23.1 g of ethyl 6-bromocaproate (b. p. 96-102° at 5 mm) was mixed with 20 g of diethylamine and 40 ml of anhydrous benzene. The separation of diethylamine hydrobromide began even at room temperature. The mixture was boiled on a water bath for 2 hours. When it had been cooled, the diethylamine hydrobromide (11.2 g, 84%) was removed by filtration and the benzene solution washed with water and dried with sodium sulfate. The residue after removal of the benzene distilled at 3 mm and 95-107°. We obtained 18.5 g of product to which 5% hydrochloric acid was added until the pH reached 3; the unreacted and insoluble ethyl bromocaproate was extracted with ether (2.9 g was obtained). The acid solution was made alkaline to pH 9 with potassium carbonate solution and the liberated oil extracted with ether; the ether solution yielded 15.3 g (81.8%) of ethyl 6-diethylaminocaproate with b. p. 103-107° (3 mm), n_D^{20} 1.439.

Found %: N 6.37, 6.41. $C_{22}H_{25}O_2N$. Calculated %: N 6.50.

Ethyl 6-N-morpholinocaproate was obtained similarly. The yield was 83.7% and the product had b. p. 140-144° (4 mm), n_D^{20} 1.458.

Found %: N 6.08. $C_{18}H_{23}O_3N$. Calculated %: N 6.10.

Ethyl 6-N-piperidinocaproate was also obtained similarly. The yield was 78.9% and the b. p. 160-164° (5 mm).

Found %: N 6.02. $C_{23}H_{25}O_2N$. Calculated %: N 6.15.

Bromomethyl ϵ -bromoamyl ketone was obtained analogously to bromomethyl δ -bromobutyl ketone, starting from 6-bromocaproyl chloride. The yield was 90% and the b. p. 115-117° (2 mm).

Found %: Br 56.83. $C_7H_{12}OBr_2$. Calculated %: Br 58.75.

ϵ -Bromoamyl 4-quinazolonyl-3-methyl ketone (V) was obtained similarly to ketone (I). The yield was 62%, allowing for the 4-quinazolone recovered. The m. p. 136-137° (from alcohol).

Found %: N 8.27, 8.60; Br 23.31. $C_{15}H_{17}O_2N_3Br$. Calculated %: N 8.31; Br 23.71.

The oxime was obtained by heating appropriate reagents in an aqueous medium for 5.5 hours on a water bath. The m. p. was 158-159°. The yield was 65.6%.

Found %: N 11.33; Br 21.31. $C_{25}H_{19}O_2N_3Br \cdot H_2O$. Calculated %: N 11.35; Br 21.54.

The dihydrochloride of ϵ -N-piperidinoamyl 4-quinazolonyl-3-methyl ketone was obtained analogously to the hydrochloride (II) from ketone (V) and piperidine. The yield was 73%. The m. p. was 204-205° (from alcohol).

Found %: N 9.57, 9.47; Cl 16.54. $C_{20}H_{27}O_2N_3 \cdot 2HCl \cdot H_2O$. Calculated %: N 9.71; Cl 16.40.

The dihydrochloride of ϵ -N-morpholinoamyl 4-quinazolonyl-3-methyl ketone was obtained analogously. The yield was 72%. The m. p. was 165-166° (from alcohol).

Found %: N 9.38; Cl 16.74. $C_{19}H_{25}O_3N_3 \cdot 2HCl \cdot H_2O$. Calculated %: N 9.68; Cl 16.32.

ϵ -N,N-Diethylaminoamyl 4-quinazolonyl-3-methyl ketone was obtained analogously to ketone (III) by heating ketone (V), diethylamine and KI in a sealed tube for 16 hours at 120-140°. The product was purified through the hydrochloride. The yield was 49%. The m. p. was 91-92.5°. The substance was soluble in acetone, benzene, alcohol and chloroform.

Found %: N 12.73, 13.00. $C_{19}H_{27}O_2N_3$. Calculated %: N 12.75.

Bromomethyl κ -bromodecyl ketone was obtained from 11-bromoundecanoyl chloride, similarly to bromomethyl bromobutyl ketone. The yield was 81.3% and the m. p. 49° (from ligroine or alcohol).

Found %: Br 47.17. $C_{12}H_{22}OBr_2$. Calculated %: Br 47.28.

κ -Bromodecyl 4-quinazolonyl-3-methyl ketones (VI) was obtained from 4-quinazalone and bromomethyl κ -bromodecyl ketone similarly to ketone (I) with the change that after the reaction, the mixture was treated with ether, into which the residual bromomethyl bromodecyl ketone passed. The crystalline precipitate was then collected, washed successively with alcohol and water and dried. The yield was 75.6% and the m. p. 90-91° (from anhydrous alcohol).

Found %: N 6.80, 6.92; Br 20.02. $C_{20}H_{27}O_2N_2Br$. Calculated %: N 6.87; Br 19.61.

The preparation of the oxime involved heating for 12 hours in an aqueous medium. The yield was 90.3%. The m. p. was 140-142°.

Found %: N 9.73, 9.79; Br 19.52. $C_{20}H_{28}N_3Br$. Calculated %: N 9.95; Br 18.96.

κ -N,N-Diethylaminodecyl 4-quinazolonyl-3-methyl ketone was obtained from ketone (VI) similarly to ketone (III). The yield was 53.8%. The m. p. was 82-83°. The product was soluble in alcohol, benzene, ether and ethyl acetate.

Found %: N 10.38. $C_{24}H_{37}O_2N_3$. Calculated %: N 10.51.

κ -N-Piperidinodecyl 4-quinazolonyl-3-methyl ketone (VII). To a solution of 3 g of ketone (VI) in 50 ml of anhydrous benzene was added 1.53 g of piperidine and the mixture boiled on a water bath for 12 hours. The piperidine hydrobromide which separated on cooling (83%) was removed, the benzene solution washed with water and the benzene removed by distillation. This yielded 1.5 g of an oil which rapidly crystallized. The m. p. was 105-106° (from anhydrous alcohol). The mother solution yielded a further 0.2 g of product. The total yield was 1.8 g (56.6%).

Found %: N 9.90, 9.85. $C_{25}H_{37}O_2N_3$. Calculated %: N 10.21.

The oxime was obtained in 60% yield. The m. p. was 120-121.5°. The product was insoluble in water, but dissolved in hot lower alcohols.

Found %: N 13.06. $C_{25}H_{39}O_2N_4$. Calculated %: N 13.13.

The dihydrochloride of κ -N-morpholinodecyl 4-quinazolonyl-3-methyl ketone was obtained analogously to the dihydrochloride (II) but with 24 hours' heating on a water bath. The yield was 50%. The m. p. was 155-157°.

Found %: N 8.80, 8.95; Cl 14.38, 14.41. $C_{24}H_{35}O_3N_3 \cdot 2HCl$. Calculated %: N 8.62; Cl 14.26.

SUMMARY

1. Methyl ω -haloalkyl ketones were smoothly brominated to give bromomethyl ω -haloalkyl ketones.
2. In the interaction of 4-quinazolone with bromomethyl ω -haloalkyl ketones, the bromomethyl group reacted to give good yields of ω -haloalkyl 4-quinazolonyl-3-methyl ketones, which reacted smoothly with diethylamine, morpholine and piperidine to form ω -N,N-diethylamino-, ω -N-morpholino- and ω -N-piperidinomethyl 4-quinazolonyl-3-methyl ketones, respectively.
3. A considerable antimalarial effect was shown by δ -N-morpholinobutyl 4-quinazolonyl-3-methyl ketone and ϵ -N-piperidinoamyl 4-quinazolonyl-3-methyl ketone.

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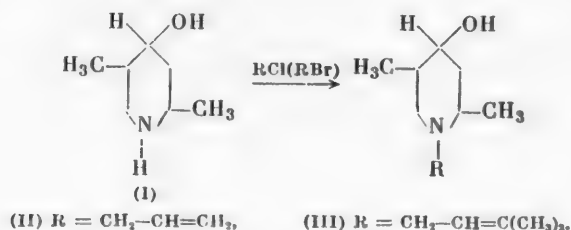
61. SYNTHETIC ANESTHETICS. XXXI. SYNTHESIS OF ESTERS OF THE β -FORM OF 1-ALKENYL-4,5-DIMETHYL-4-PIPERIDOLS

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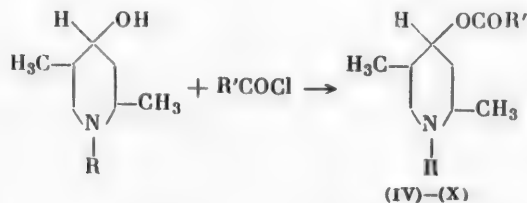
In a previous communication [1] we described various esters of the α -form of secondary 1-alkenyl-2,5-dimethyl-4-piperidols and most of these showed a high anesthetic activity. We synthesized a series of new esters of the β -form of secondary 1-alkenyl-2,5-dimethyl-4-piperidols in order to elucidate the effect of the steric structure and the character of the acyl group on the pharmacological properties of these compounds.

The starting 1-alkenyl-2,5-dimethyl-4-piperidols (II) and (III) were obtained in high yields (70-80%) by alkylation of the β -form of 2,5-dimethyl-4-piperidol (I) [2, 3] with appropriate halogen derivatives of the allyl type in benzene solution, using 1 mole of the halogen derivative to 2 moles of piperidol.



The second molecule of piperidol (I) used in the reaction was consumed in binding the hydrogen halide liberated to form the hydrohalide salt, as in the alkylation of dimethylpiperidone under analogous conditions, and was recovered by treatment with alkali [4].

The secondary 1-alkenyl-2,5-dimethyl-4-piperidols (II) and (III) obtained were esterified with the acid chlorides of various acids to yield seven new esters (IV)-(X), which are given in Table 1.



Of the seven esters of the β -form of 1-alkenyl-2,5-dimethyl-4-piperidols synthesized, six [(IV)-(VII), (IX) and (X)] were examined for anesthetic activity in the form of their hydrochlorides in the Pharmacology Department of the G. I. Samarina State Medical Institute, Kazan. The anesthesia indices of novocaine, cocaine and daine at

the same concentrations were used for comparing the local anesthetic activity of these esters. The phenoxyacetates of 1-allyl- and 1-(γ, γ -dimethylallyl)-2,5-dimethyl-4-piperidols, (V) and (VII), had a weak anesthetic action, while the other esters showed a high activity and low toxicity. The main results of the pharmacological examination are presented in Table 2.

EXPERIMENTAL*

The piperidols and their esters synthesized in the present work were derivatives of the β -isomer of 2,5-dimethyl-4-piperidol with m. p. 140-141°, which was described previously [2, 3].

1-Allyl-2,5-dimethyl-4-piperidol (II). A solution of 10.16 g of allyl bromide in 20 ml of benzene was added over a period of 30 minutes with stirring to a solution of 18.1 g of the β -form of 2,5-dimethyl-4-piperidol in 450 ml of dry benzene on a water bath at 75°. The mixture was kept at 70-75° and stirred for 7 hours. The precipitated hydrobromide of the original piperidol (15.75 g) was removed by filtration and washed with benzene and dry ether. The benzene was removed under reduced pressure, the residue dissolved in dry ether and the small amount of the precipitated hydrobromide removed by filtration. The ether was evaporated and the residue vacuum distilled. We obtained 8.45 g (71%) of the β -form of 1-allyl-2,5-dimethyl-4-piperidol (II) as a very thick oil with b. p. 98° (4 mm), n_D^{20} 1.4900.

Found %: N 8.57, 8.62. $C_{10}H_{19}ON$. Calculated %: N 8.28.

The hydrochloride was obtained by the action of an ether solution of hydrogen chloride on an anhydrous alcohol solution of the piperidol and was a difficultly crystallizable, hygroscopic compound with m. p. 114-115° (from a mixture of alcohol and ether).

Found %: N 6.55, 6.47; Cl 17.15, 17.16. $C_{10}H_{19}ONCl$. Calculated %: N 6.81; Cl 17.23.

1-(γ, γ -Dimethylallyl)-2,5-dimethyl-4-piperidol (III). A solution of 6.9 g of γ, γ -dimethylallyl chloride [5] was added dropwise with stirring over a period of 10 minutes to a solution of 12.9 g of the β -form of 2,5-dimethyl-4-piperidol in 300 ml of dry benzene on a water bath at 74°. The reaction mixture was stirred at 70-75° for 14 hours. The precipitate was removed by filtration and washed with benzene and dry ether; we obtained 8.28 g of the hydrochloride of the original piperidol with m. p. 205-207°. The benzene solution was

treated as in the previous experiment and the piperidol vacuum distilled. We obtained 8 g (81%) of the β -form of 1-(γ, γ -dimethylallyl)-2,5-dimethyl-4-piperidol (III) as a thick colorless oil, which rapidly set to crystals. The b. p. was 114° (3 mm) and the m. p. 68.5-70° (from ligroine in the form of coarse cubic crystals in 70% yield).

Found %: N 7.25, 7.04. $C_{12}H_{23}ON$. Calculated %: N 7.10.

The hydrochloride was a difficultly crystallizable, hygroscopic compound with m. p. 119-121° (from a mixture of alcohol and ether).

Found %: N 5.69, 5.75; Cl 15.03, 15.25. $C_{12}H_{23}ONCl$. Calculated %: N 5.99; Cl 15.16.

The base was liberated from the hydrochloride (hydrobromide) of the original piperidol, recovered from the reaction, by the action of 50% sodium hydroxide solution on an aqueous solution of the salt. The precipitate was collected on a Schott funnel, dried in a desiccator and recrystallized from ligroine (80-100° fraction).

TABLE 1

Ester	R	R'
(IV)	$CH_2CH=CH_2$	C_6H_5
(V)	$CH_2CH=CH_2$	$C_6H_5OCH_2$
(VI)	$CH_2CH=OCH_3$	C_6H_5
(VII)	$CH_2CH=OCH_3$	$C_6H_5OCH_2$
(VIII)	$CH_2CH=OCH_3$	$C_6H_5CH_2$
(IX)	$CH_2CH=OCH_3$	$C_6H_5CH_2CH_2$
(X)	$CH_2CH=OCH_3$	$C_6H_5CH=CH$

TABLE 2

Anesthetic Activity and Toxicity

Ester tested	Anesthesia index in Rene units				Minimum lethal dose (in mg/g)
	concentration (in%)				
	0.25	0.5	1.0	2.0	
Novocaine	109	181	255	309	0.3
Cocaine	158	401	573	733	0.15
Dicaine	1182	1194	1289	1333	—
(IV)	245	399	1123	1333	0.3
(V)	78	79	84	143	0.5
(VI)	1123	885	1131	1217	0.3
(VII)	73	83	107	132	0.1
(IX)	603	1233	1298	1333	0.3
(X)	1013	1252	1291	1296	0.2

*M. Eskalrov, T. Sokol'skaya, and T. Baranova participated in the experimental work.

From 8.28 g of the hydrochloride we obtained 6 g (93%) of the β -form of 2,5-dimethyl-4-piperidol with m. p. 140-141°.

Benzoate of 1-allyl-2,5-dimethyl-4-piperidol (IV). To a solution of 3.39 g of the β -form of 1-allyl-2,5-dimethyl-4-piperidol (II) in 10 ml of dry pyridine was added 8.44 g of benzoyl chloride. The reaction mixture was heated on a glycerol bath at 100-105° for 4 hours. On the following day the hydrochloride was precipitated with dry ether, collected by filtration, washed with ether and dried in a desiccator. Two recrystallizations from benzene yielded 5.3 g (85%) of the benzoate of the β -form of 1-allyl-2,5-dimethyl-4-piperidol hydrochloride (IV) as white, attached needles with m. p. 197.5-198°.

Found %: N 4.43, 4.45; Cl 11.31, 11.22. $C_{17}H_{24}O_2NCl$. Calculated %: N 4.52; Cl 11.44.

Phenoxyacetate of 1-allyl-2,5-dimethyl-4-piperidol (V). To a solution of 1.7 g of the β -form of 1-allyl-2,5-dimethyl-4-piperidol in 10 ml of dry benzene was added 0.12 g of finely cut magnesium turnings and a solution of 5.12 g of phenoxyacetyl chloride in 10 ml of dry benzene [6]. The mixture was heated on a glycerol bath at 90-95° for 10 hours. The thick yellow oil liberated was separated and washed with dry ether and on drying in a vacuum desiccator, it solidified; the weight was 1.5 g. After unsuccessful attempts to purify the product by recrystallization, we treated it with sodium carbonate solution and extracted the liberated base with ether. The extract was dried with sodium sulfate, the ether removed and the residue vacuum distilled. We obtained 1.15 g (~38%) of the phenoxyacetate of the β -form of 1-allyl-2,5-dimethyl-4-piperidol (V) as a thick liquid with b. p. 164-166° (2 mm), n_D^{20} 1.5145.

Found %: N 4.70, 4.73. $C_{18}H_{25}O_3N$. Calculated %: N 4.62.

The hydrochloride formed fine, needlelike crystals with m. p. 159-160° (from a mixture of anhydrous alcohol and absolute ether).

Found %: N 4.26, 4.27; Cl 10.14, 10.09. $C_{13}H_{26}O_3NCl$. Calculated %: N 4.12; Cl 10.43.

Benzoate of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol (VI). A solution of 2.96 g of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol in 10 ml of pyridine was heated with 3.33 g of benzoyl chloride for 2 hours on a glycerol bath at 100-105°. When the mixture had cooled, 3 g of benzoyl chloride was added and the mixture heated at 100-105° for a further 2 hours. The next day, the precipitate of coarse white crystals was collected and washed with pyridine and dry ether. The addition of dry ether to the mother solution precipitated a brown material which was also collected. Recrystallization of the two precipitates from benzene yielded 4.3 g (85%) of the benzoate of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol hydrochloride (VI) as lustrous plates with m. p. 195-196°.

Found %: N 4.20, 4.26; Cl 10.18, 10.28. $C_{19}H_{28}O_2NCl$. Calculated %: N 4.15; Cl 10.49.

Phenoxyacetate of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol (VII). To a solution of 2 g of the β -form of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol in 10 ml of dioxane were added 0.12 g of magnesium and 5.5 g of phenoxyacetyl chloride. The mixture was heated at 100-105° for 8 hours. The reaction mixture which had a voluminous precipitate was diluted with dry ether and the precipitate collected and dried (3.25 g). Recrystallization from dry acetone yielded 2.5 g (70%) of the phenoxyacetate of the β -form of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol (VII) as fine needles with m. p. 182-183°.

Found %: N 3.52, 3.85; Cl 9.66, 9.54. $C_{20}H_{30}O_3NCl$. Calculated %: N 3.81; Cl 9.64.

Phenylacetate of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol (VIII). A solution of 1.97 g of the β -form of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol in 25 ml of dry benzene was heated with 2.02 g of phenylacetyl chloride and 0.12 g of magnesium at 90° for 10 hours. The benzene was removed, the residue treated with a saturated sodium carbonate solution, the liberated base extracted with ether and the ether solution washed with water and dried with sodium sulfate. The ether was removed and the residue vacuum distilled. We obtained 1.89 g (60%) of the phenylacetate of the β -form of 1-(γ,γ -dimethylallyl)-2,5-dimethyl-4-piperidol (VIII).

B. p. 191-192° (2 mm), n_D^{20} 1.5110, d_4^{20} 1.0022, MR 94.43; Calc. 93.77.

Found %: N 4.87, 4.75. $C_{20}H_{29}O_2N$. Calculated %: N 4.44.

The picrate formed yellow, needlelike crystals with m. p. 127-128° (from anhydrous alcohol).

Found %: N 10.43, 10.10. $C_{26}H_{32}O_9N_4$. Calculated %: N 10.29.

The hydrochloride was an uncrystallizable liquid.

Hydrocinnamate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol (IX). 2.77 g of the β -form of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol in 10 ml of dioxane and 7.08 g of hydrocinnamyl chloride were heated at 100-105° for 9 hours. The reaction product was precipitated with dry ether and recrystallized from benzene. We obtained 3.4 g (65.4%) of the hydrocinnamate of the β -form of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol hydrochloride (IX) as fine needles with m. p. 124-125°.

Found %: N 3.58, 3.68; Cl 10.35, 10.20. $C_{21}H_{28}O_2NCl$. Calculated %: N 3.83; Cl 9.70.

The hydrocinnamate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol as the free base was a mobile liquid.

B. p. 187-189° (2 mm), n_D^{20} 1.5120, d_4^{20} 1.0015, MR 98.58; Calc. 98.39.

Found %: N 4.48, 4.54. $C_{21}H_{28}O_2N$. Calculated %: N 4.25.

The picrate formed yellow crystals with m. p. 86-87° (from anhydrous alcohol).

Found %: N 9.98; 9.87. $C_{27}H_{34}O_9N_4$. Calculated %: N 10.03.

Cinnamate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol (X). 2 g of the β -form of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol in 10 ml of dioxane, 0.12 g of magnesium and 5 g of cinnamyl chloride in 10 ml of dioxane were heated at 100-105° for 8 hours. The precipitate that formed was collected and the rest of the hydrochloride precipitated from the filtrate with dry ether and collected. Recrystallization from acetone yielded 3 g (83%) of the cinnamate of the β -form of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol hydrochloride (X) as needlelike crystals with m. p. 204-206°.

Found %: N 3.97, 4.01; Cl 9.44, 9.64. $C_{21}H_{28}O_2NCl$. Calculated %: N 3.85; Cl 9.75.

The cinnamate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol as the free base was a thick, viscous liquid with b. p. 210-212° (2 mm).

Found %: N 4.32, 4.48. $C_{21}H_{28}O_2N$. Calculated %: N 4.28.

The picrate formed yellow, attached needlelike crystals with m. p. 163-164° (from anhydrous alcohol).

Found %: N 10.43, 10.51. $C_{27}H_{32}O_9N_4$. Calculated %: N 10.07.

SUMMARY

1. Alkenylation of the β -form of 2,5-dimethyl-4-piperidol with allyl bromide and γ , γ -dimethylallyl chloride gave high yields (70-80%) of the β -forms of 1-allyl- and 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidols.

2. The following esters were synthesized by esterification of these piperidols with the acid chlorides of various acids: The benzoate and phenoxyacetate of 1-allyl-2,5-dimethyl-4-piperidol and the benzoate, phenoxyacetate, hydrocinnamate and cinnamate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol. Six esters (all but the phenylacetate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol) were examined pharmacologically. Of them, the phenoxyacetates of 1-allyl- and 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidols showed a weak anesthetic activity, while the other four, i.e., the benzoate of 1-allyl-2,5-dimethyl-4-piperidol and the benzoate, hydrocinnamate and cinnamate of 1-(γ , γ -dimethylallyl)-2,5-dimethyl-4-piperidol, showed an anesthetic activity which was several times greater than that of novocaine and cocaine and had a comparatively low toxicity.

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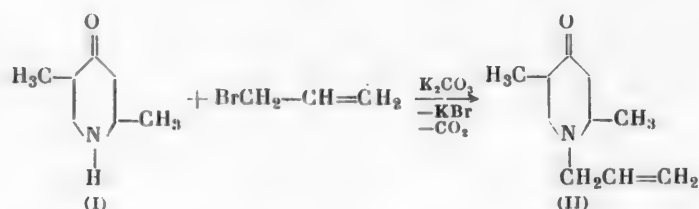
62. SYNTHESIS OF 1-ALKENYL-2,4,5-TRIMETHYL-4-PIPERIDOLS

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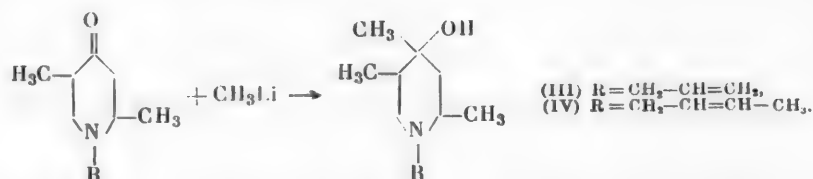
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In a previous communication [1], we described the synthesis of 1-alkenyl-2,5-dimethyl-4-ethyl-4-piperidols, whose esters showed a high anesthetic activity. In order to elucidate the effect of the size of the substituent at C₄ of the piperidine ring on the pharmacological properties of the compounds, we synthesized the 1-alkenyl-2,4,5-trimethyl-4-piperidols (III) and (IV). The esters of these piperidols and their pharmacological properties will be described in a subsequent communication.

One of the starting compounds, 1-allyl-2,5-dimethyl-4-piperidone (II), which has been described previously [2, 3], we obtained in high yield (~88%) by heating 1 mole of 2,5-dimethyl-4-piperidone (I) with 1 mole of allyl bromide (chloride) in acetone or butanol-1 in the presence of potassium or sodium carbonate (to bind the hydrogen halide liberated during the reaction).



The interaction of the methyl lithium [4] with 1-alkenyl-2,5-dimethyl-4-piperidones gave high yields (~85%) of 1-alkenyl-2,4,5-trimethyl-4-piperidols (III) and (IV) as uncrystallizable mixtures of stereoisomers, as in the case of the reaction with ethyllithium [1].



For separation of the individual isomers, the mixtures were converted into the hydrochlorides and the individual hydrochlorides were isolated by fractional crystallization of the crystalline salts obtained. From the mixture of stereoisomeric 1-allyl-2,4,5-trimethyl-4-piperidols (III), we isolated one individual hydrochloride, from which the individual base was obtained as low-melting crystals. The mixture of stereoisomeric 1-crotyl-2,4,5-trimethyl-4-piperidols (IV) also yielded one individual hydrochloride from which the individual base was isolated as low-melting, needle-like crystals.

The rest of the mixtures of isomers of the hydrochlorides of both piperidols (III) and (IV) were obtained as uncrystallizable liquids.

EXPERIMENTAL *

1-Allyl-2,5-dimethyl-4-piperidone (II). To a solution of 31.9 g of 2,5-dimethyl-4-piperidone (I) in 60 ml of dry acetone was added 69 g of anhydrous potassium carbonate as a powder and a solution of 33.3 g of allyl bromide in 15 ml of acetone was added dropwise to the mixture on a water bath at 60° with vigorous stirring. The mixture was stirred vigorously at 70-75° for 6 hours. The precipitate removed and washed carefully with acetone. The acetone and unreacted allyl bromide were removed under reduced pressure. The residue was treated with 50% sodium hydroxide solution, the base extracted with ether and the ether solution dried with potassium carbonate. The ether was removed and the residue vacuum distilled from a flask with a fractionating head. We obtained 36.8 g (~88%) of 1-allyl-2,5-dimethyl-4-piperidone with b. p. 79-81° (3 mm), n_D^{20} 1.4740.

1-Allyl-2,4,5-trimethyl-4-piperidol (III). The reaction was carried out in a three-necked flask fitted with a mechanical stirrer with a mercury seal, a reflux condenser and a dropping funnel with calcium chloride tubes, with vigorous stirring in an atmosphere of dry nitrogen. To 5.1 g of finely cut lithium in 100 ml of absolute ether was added 46.85 g of freshly distilled methyl iodide. About 40 drops of methyl iodide was added first so as to start the reaction and the rest of the methyl iodide was dissolved in 100 ml of absolute ether and added dropwise over a period of 2.5 hours so that the ether boiled gently. The mixture was then heated for 3 hours. A solution of 33.46 g of 1-allyl-2,5-dimethyl-4-piperidone in 90 ml of absolute ether was added dropwise over a period of 1 hour to the solution of methyllithium obtained with cooling in ice water. Stirring was continued for a further 30 minutes and the reaction mixture was left overnight in a nitrogen atmosphere. The mixture was heated for 8.5 hours on the following day. The alcoholate formed was decomposed with water with cooling. The ether layer was separated and the aqueous alkali one extracted many times with ether. The combined ether solutions were washed with a saturated solution of sodium chloride and dried with potassium carbonate. The ether was removed and the residue vacuum distilled. We obtained 31.1 g (85%) of a mixture of stereoisomeric 1-allyl-2,4,5-trimethyl-4-piperidols (III) as a thick liquid.

B. p. 95-96° (4 mm), n_D^{20} 1.4840, d_4^{20} 0.9461, MR 55.43; Calc. 55.80.

Found %: N 7.61, 7.80. $C_{11}H_{21}ON$. Calculated %: N 7.64.

24 g of the mixture of isomeric piperidols was dissolved in anhydrous alcohol and an ether solution of hydrogen chloride was added with cooling until an acid reaction was produced. Recrystallization of the precipitate from acetone yielded 10.3 g (~36% of the total mixture of isomers) of an individual hydrochloride of 1-allyl-2,4,5-trimethyl-4-piperidol with m. p. 177-179°.

Found %: N 6.54, 6.44; Cl 15.91, 16.04. $C_{11}H_{22}ONCl$. Calculated %: N 6.37; Cl 16.14.

The hydrochloride was treated with a saturated solution of sodium carbonate and the liberated base extracted with ether; we obtained an individual isomer of the base as a low-melting crystalline substance (m. p. 29-30°).

Found %: N 7.91, 7.95. $C_{11}H_{21}ON$. Calculated %: N 7.64.

1-Crotyl-2,4,5-trimethyl-4-piperidol (IV). As in the previous experiment, to 6.1 g of lithium in 100 ml of absolute ether was added 57.1 g of methyl iodide in 100 ml of absolute ether over a period of 4 hours. The mixture was then heated for 3 hours. With cooling in ice water, a solution of 40.4 g of 1-crotyl-2,5-dimethyl-4-piperidone (n_D^{20} 1.4765) in 100 ml of absolute ether was added over 1 hour to the methyllithium obtained. The mixture was stirred for a further 30 minutes, left overnight in a nitrogen atmosphere and heated for 8.5 hours on the following day. The reaction mixture was then treated as in the previous experiment. After removal of the ether, the residue was vacuum distilled; we obtained 37.6 g (85.5%) of a mixture of stereoisomers of 1-crotyl-2,4,5-trimethyl-4-piperidol as a thick liquid with b. p. 97-99° (3 mm), n_D^{20} 1.4855.

Found %: N 6.99, 7.17. $C_{12}H_{23}ON$. Calculated %: N 7.10.

31.8 g of the mixture of isomeric piperidols was dissolved in absolute alcohol and converted into the salts by the action of an ether solution of hydrogen chloride. Fractional recrystallization of the salt isolated yielded

* The students T. Sadykov and O. Komanova participated in the experimental work.

from a mixture of acetone and alcohol 4.5 g (~12% of the total mixture) of an individual hydrochloride of 1-crotyl-2,4,5-trimethyl-4-piperidol with m. p. 169-171°.

Found %: N 5.98, 5.75; Cl 14.50, 14.34. $C_{12}H_{24}ONCl$. Calculated %: N 5.99; Cl 15.16.

The base of the individual isomer formed low-melting, needlelike crystals.

SUMMARY

1. The interaction of 1 mole of 2,5-dimethyl-4-piperidone with 1 mole of allyl bromide (chloride) in acetone (butanol-1) in the presence of potassium carbonate (sodium carbonate) gave 1-allyl-2,5-dimethyl-4-piperidone in a yield of ~88% on the original piperidone.

2. The interaction of methylolithium with 1-allyl- and 1-crotyl-2,5-dimethyl-4-piperidones gave ~85% yield of 1-allyl- and 1-crotyl-2,4,5-trimethyl-4-piperidols as uncrystallizable mixtures of stereoisomers. Fractional crystallization of their hydrochlorides yielded one individual isomer of each.

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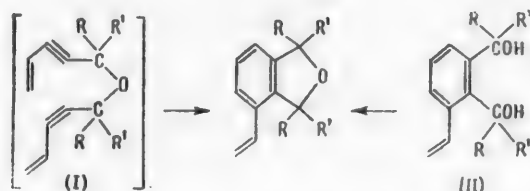
MECHANISM OF THE CONVERSION OF VINYLETHYNYLCARBINOLS INTO VINYLISOCOUMARANS

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In previous work [1] we showed that when vinyl ethynylcarbinols are heated with acids or, better, ferric chloride, they dimerize to vinylisocoumarans with the elimination of a water molecule.

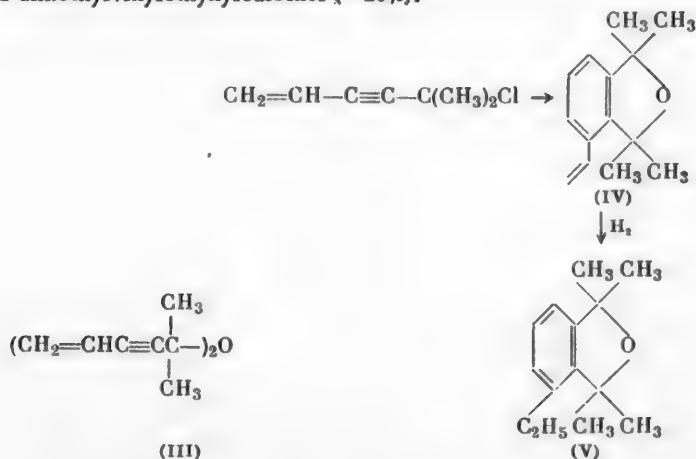
The hypothesis was put forward that the reaction proceeds through the formation of the intermediate ether (I), which then undergoes intramolecular cyclization. We also cannot exclude the possibility of the initial formation of the aromatic system (by a type of diene synthesis) with subsequent elimination of a water molecule from the glycol (II).



As a series of authors showed [2], it is by precisely this scheme that vinylacetylene hydrocarbons are dimerized into styrene derivatives, though this is always achieved only by heating.

In the present work we undertook to determine the course of the reaction, in particular, to solve the problem of whether cyclization precedes the formation of the ether link, or, on the contrary, the formation of the latter is the first stage of the reaction.

For this purpose we attempted to prepare the ether from dimethylvinylethynylcarbinol by the action of silver carbonate on dimethylvinylethynylchloromethane at 0° in ether, i.e., under such mild conditions that the cyclization by the second scheme was impossible, since it requires an elevated temperature. However, instead of the desired ether (III), we isolated tetramethylvinylisocoumaran (IV) in 10% yield together with vinylisopropenylacetylene (~15%) and dimethylvinylethynylcarbinol (~18%).

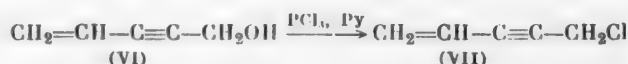


Since we could not exclude the possibility that ether (III) could undergo cyclization even during distillation a special experiment was carried out in which the reaction mixture was hydrogenated in the cold in the presence of magnesium oxide (to neutralize the hydrogen chloride liberated by hydrogenation of the excess chloride). In this case also we obtained only tetramethylethylisocoumaran (V) and not the ether from dimethylbutylcarbinol, i. e., the hydrogenation product of ether (III).

We also used another well known method of preparing ethers, namely the interaction of alcoholates with alkyl halides. In this case also, the reaction of dimethylvinylethynylchloromethane with the magnesium alcoholate of dimethylvinylethynylcarbinol yielded only the isocoumaran (IV); the corresponding ether was not detected.

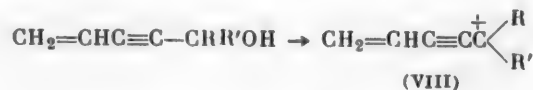
The results obtained leave hardly any doubt that the first stage of the reaction is the formation of the ether link. This is in accordance with the fact that up to now it has not been possible to convert the methyl and propyl ethers of dimethylvinylethynylcarbinol into aromatic derivatives.

Thus, the hydroxyl group of the carbinol is the reactive center, which is attacked in the first instance and, consequently, its lability must determine the course of the reaction. Actually, tertiary vinylethynylcarbinols with the most labile hydroxyl group give the highest yields of isocoumarans (40-60%), while secondary carbinols, where the lability of the hydroxyl is less, give low yields (20-25%). From this point of view, it seemed interesting to investigate the behavior of the primary alcohol vinylethynylcarbinol (VI). It was found that even on prolonged heating with ferric chloride, vinylethynylcarbinol (VI) hardly changed and this can be explained only by the relatively low lability of the hydroxyl. The latter also appears in other reactions. While dimethylvinylethynylcarbinol readily forms a chloride when shaken with hydrochloric acid [3], carbinol (VI) does not react under these conditions. The corresponding chloride (VII) was obtained by the action of phosphorus trichloride on carbinol (VI) in the presence of pyridine.

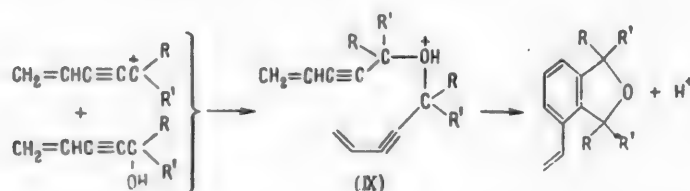


The structure of the chloride (VII) was confirmed by hydrolysis to carbinol (VI) by the action of potassium acetate in methanol. It should be noted that the usual method of hydrolysis with alkali produced complete decomposition of the carbinol to vinylacetylene, methanol and formic acid. The chlorine atom in chloride (VII) is relatively unlabile: A weak turbidity appeared only after 15-20 minutes with a solution of silver nitrate, while dimethylvinylethynylchloromethane reacted completely in a few seconds. Attempts to prepare the corresponding isocoumaran by the action of silver carbonate on chloride (VII) and also the action of the magnesium alcoholate of carbinol (VI) on it did not lead to the desired result.

The results obtained make it possible to represent the mechanism of the reaction in the following way. Ferric chloride forms a complex of the Lewis's acid type with the carbinol, $(\text{RO}\cdots\text{FeCl}_2)^+\text{H}^+$, which produces (at an elevated temperature) elimination of the hydroxyl and formation of a carbonium ion (VIII).

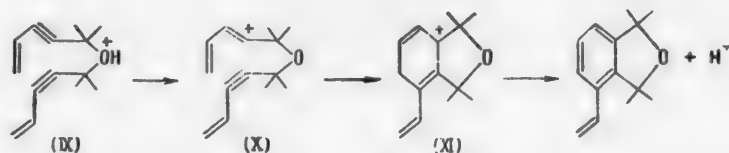


This ion reacts with another molecule of carbinol to form the onium complex (IX), which undergoes cyclization with the preliminary or subsequent elimination of a proton.

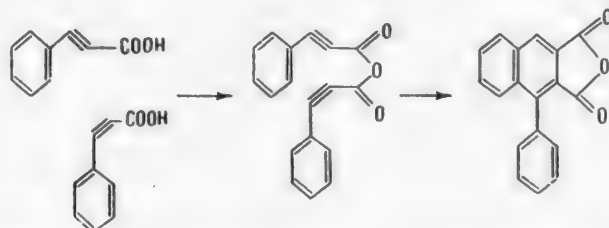


The same ion (VIII) is evidently produced also by the action of silver carbonate on dimethylvinylethynylchloromethane, initiating the same cyclization reaction.

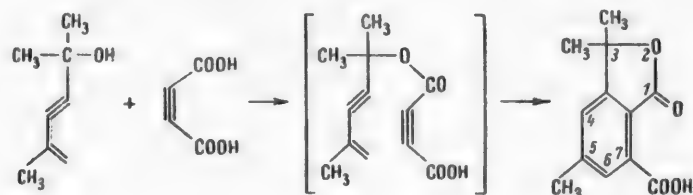
The actual cyclization reaction, which is the second stage of the formation of isocoumarans, is an intramolecular diene synthesis reaction, accompanied by migration of hydrogen (in the form of a proton). It is quite possible to suppose that the intermediate ion (IX) rearranges into ion (X), whose diene system, due to its proximity, reacts with the triple bond to form ion (XI), giving (with transposition of a double bond and elimination of a proton) an aromatic system.



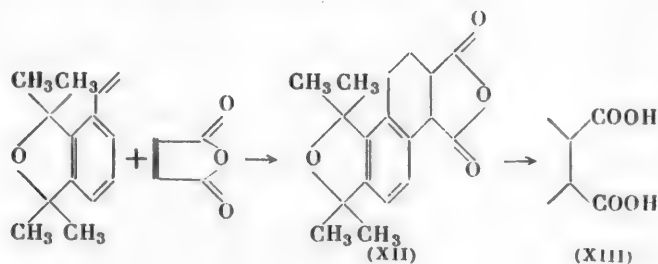
The cyclic dimerization of vinyl ethynylcarbinols is very similar to the dimerization of phenylpropionic acid and its derivatives into α -phenylnaphthalene derivatives [4]. This is achieved by heating with acetic anhydride and undoubtedly proceeds through the stage of anhydride formation. The anhydride was obtained specially and was found to cyclize extremely readily on heating or on irradiation.



Another interesting case is the condensation of acetylenedicarboxylic acid with dimethylpropenylethynylcarbinol, which leads to the formation of 3,3,5-trimethylphthalide-7-carboxylic acid, and the formation of an intermediate ester has been proposed here similarly [5].



For complete characterization of 1,1,3,3-tetramethyl-4-vinylisocoumaran as a styrene derivative, we condensed it with maleic anhydride. The reaction could be accomplished only at 160–170°, when the corresponding adduct (XII) was obtained in 45% yield, and this gave the dicarboxylic acid (XIII).



EXPERIMENTAL

Action of silver carbonate on dimethylvinylethynylchloromethane.* The silver carbonate was obtained by mixing solutions of silver nitrate and potassium carbonate. The precipitate was collected by filtration, washed

*Ditertiary-butyl ether was obtained in 35% yield by this method [6].

with water, alcohol and ether and dried to constant weight in vacuum at 35-40°.

Dimethylvinylethynylchloromethane was obtained by the action of hydrogen chloride on dimethylvinylethynylcarbinol and had b. p. 32° (10 mm) and n_D^{20} 1.4790.

a) To a suspension of 71.5 g of freshly prepared dry silver carbonate in 200 ml of absolute ether was added 65.5 g of freshly distilled dimethylvinylethynylchloromethane over a period of 1 hour with stirring at 0°, when the evolution of heat was observed and the temperature rose by 2-3°. The mixture was then stirred at 0° for 19 hours and filtered and the reaction product vacuum distilled. As a result of two distillations, we obtained 6 g (~15%) of vinylisopropenylacetylene with b. p. 40-45° (80 mm, and n_D^{20} 1.4990; 7 g of dimethylvinylethynylchloromethane with b. p. 30-33° (10 mm) and n_D^{20} 1.4820; 8 g (18%) of dimethylvinylethynylcarbinol with b. p. 58-59° (13 mm) and n_D^{20} 1.4800 and 4.5 g (10%) 1,1,3,3-tetramethylvinylisocoumaran (IV) with b. p. 79.5-80° (2.5 mm), n_D^{20} 1.5252. The isocoumaran (IV) was identified through the dibromide with m. p. 109°, which did not depress the melting point of an authentic sample.

b) An analogous experiment was carried out with the same amounts of reagents. When the reaction mixture had been stirred (19 hours, 0°) and filtered, to the ether solution of the reaction products, diluted with 100 ml of ether, was added 10 g of magnesium oxide and the mixture hydrogenated in the presence of Adam's catalyst at first at 0° and then at 20°. After 27 hours, 30 liters of hydrogen had been absorbed, while fresh catalyst was added several times during this period. The mixture was then transferred to a rotating autoclave and hydrogenated at 20° in the presence of Raney nickel under 90 atm for 10 hours, when a further 2.5 liters of hydrogen was absorbed. After filtration and removal of the ether, the reaction product was distilled at first at normal pressure and then in vacuum. As a result of 2 distillations we obtained: 6 g (~14%) of 2-methylhexane with b. p. 89-90° and n_D^{20} 1.3860; 7 g (~16%) of 2-methylhexanol-2 with b. p. 130-140° and n_D^{20} 1.4185 and 6.5 g (13%) of 1,1,3,3-tetramethyl-4-ethylisocoumaran (V) with b. p. 94-96° (7 mm), n_D^{20} 1.4900, which crystallized on cooling to give crystals with m. p. 24-24.5°, which did not depress the melting point of an authentic sample.

Interaction of the alkoxymagnesium bromide from dimethylvinylethynylcarbinol with dimethylvinylethynylchloromethane. To a solution of ethylmagnesium bromide obtained from 12 g of magnesium, 60 g of ethyl bromide and 175 ml of absolute ether, was added 110 g of dimethylvinylethynylcarbinol over a period of 30 minutes with cooling and stirring so that the temperature did not rise above 10°. The mixture was stirred for 1 hour at 20°, the ether removed, the thick mass diluted with 20 g of dimethylvinylethynylcarbinol and 64.5 g of dimethylvinylethynylchloromethane added in 10 g portions at 50-70° over a period of 3.5 hours with vigorous stirring. The cooled reaction mixture was decomposed first with 100 ml of ice water and then with 300 ml of 6% hydrochloric acid. The product was extracted with ether, dried and distilled. As a result of two distillations we isolated 8 g of the original chloride with b. p. 20-26° (17 mm), n_D^{20} 1.4790; 101.5 g of dimethylvinylethynylcarbinol with b. p. 56-61° (17 mm), n_D^{20} 1.4780 and 27.5 g (31%) 1,1,3,3-tetramethyl-4-vinylisocoumaran (IV) with b. p. 79-83° (2.5 mm), n_D^{20} 1.5266. The isocoumaran (IV) was identified as usual through the dibromide.

Preparation of vinyleneethynylchloromethane. Vinyleneethynylcarbinol was obtained by the action of formaldehyde on vinylacetylenylmagnesium bromide. It had b. p. 60-62° (13 mm), n_D^{22} 1.4960.

Over a period of 2 hours, a solution of 63 g of vinyleneethynylcarbinol in 30 ml of anhydrous pyridine was added to 42.5 g of phosphorus trichloride while the temperature was kept at 5-7°. The mixture was stirred for a further 1 hour at 0° and then the volatile substances were vacuum distilled at 50-60 mm and 50-53° with the receiver cooled to -10°. The distillate was washed twice with water, dried with potassium carbonate and distilled in the presence of 0.1 g of hydroquinone. We obtained 49 g (64%) of vinyleneethynylchloromethane.

B. p. 50-51° (50 mm), n_D^{20} 1.5020, d_4^{20} 1.0136, MR 29.26; Calc. 27.69.

Found %: Cl 34.95, 34.85. C_5H_5Cl . Calculated %: Cl 35.29.

The chloride was a colorless, mobile liquid, which rapidly became yellow and turbid when stored. It gave a weak turbidity with an aqueous alcohol solution of silver nitrate only after 15-20 minutes and formed a voluminous precipitate after 20 hours.

Hydrolysis of vinyleneethynylchloromethane. A mixture of 10 g of vinyleneethynylchloromethane, 13 g of potassium acetate and 75 ml of methanol was boiled under reflux until the separation of potassium chloride ceased (45 hours). The methanol was removed under reduced pressure and the residue diluted with 10 ml of water and extracted with

ether. As a result of 2 distillations we obtained 3.5 g (50%) of vinyl ethynylcarbinol with b. p. 66.5-67° (16 mm), n_D^{20} 1.4940.

Action of silver carbonate on vinyl ethynylchloromethane. 30 g of vinyl ethynylchloromethane, 40 g of freshly prepared silver carbonate and 150 ml of absolute ether were stirred for 19 hours at 0° and then boiled under reflux for 15 hours. By the usual processing and distillation we recovered 26 g of the original chloride with b. p. 49.5-50° (47 mm), n_D^{20} 1.5005, and 1 g of a polymeric residue

The corresponding isocoumaran could not be detected either in the products from the action of the alkoxy-magnesium bromide on vinyl ethynylchloromethane.

Condensation of 1,1,3,3-tetramethyl-4-vinylisocoumaran with maleic anhydride. A mixture of 15 g of isocoumaran (IV), 7.2 g of maleic anhydride and 7 ml of xylene was heated under reflux for 2 hours at 160-170°. The whole mass crystallized on cooling. Recrystallization from benzene yielded 5 g of the anhydride of 1,1,3,3-tetramethyl-1,3,6,7,8,9-hexahydronaphthofuran-8,9-dicarboxylic acid (XII) with m. p. 236-238°.

Found %: C 72.05, 71.63; H 6.66, 6.48. M 297, 302 (titration with 0.1 N NaOH). $C_{18}H_{20}O_4$. Calculated %: C 72.00; H 6.66. M 300.

The mother solution was evaporated to dryness and the solid residue powdered and heated for 1 hour at 100° with 75 ml of 10% sodium hydroxide. Filtration and acidification yielded 5 g of the dicarboxylic acid (XIII) as a fine white powder with m. p. 224-237° (decomp.). The total yield of the condensation product was 45%. Similarly, 0.85 g of pure anhydride (XII) yielded 0.7 g of acid (XIII) with m. p. 236-238° (decomp.).

Found %: C 67.98, 67.67; H 7.26, 7.01. M 314 (titration). $C_{18}H_{22}O_5$. Calculated %: C 67.92; H 6.92; M 318.

1.3 g of anhydride (XII) and 7 ml of absolute methanol were boiled for 7 hours until solution was complete. Evaporation to dryness and recrystallization from a mixture of benzene and ligroine yielded 0.55 g of the mono-methyl ester of acid (XIII) with m. p. 154-155°.

Found %: C 68.62, 68.45; H 7.35, 7.38. $C_{19}H_{24}O_5$. Calculated %: C 68.67; H 7.23.

SUMMARY

1. It was found that cyclic dimerization of compounds of the vinyl ethynylcarbinol type into isocoumarans occurs not only when vinyl ethynylcarbinols are heated with ferric chloride, but also when dimethylvinyl ethynylchloromethane reacts with silver carbonate or an alcoholate of dimethylvinyl ethynylcarbinol.

2. The first stage of the cyclic dimerization is the formation of the ether link. Then intramolecular diene condensation occurs with migration of hydrogen and the formation of an aromatic system. The course of the reaction is thus determined by the lability of the hydroxyl group. In agreement with this, vinyl ethynylcarbinol, where the hydroxyl group is least labile, was found to be incapable of cyclic dimerization.

3. 1,1,3,3-Tetramethyl-4-vinylisocoumaran reacts with maleic anhydride to form the normal product of diene synthesis.

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INTERACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

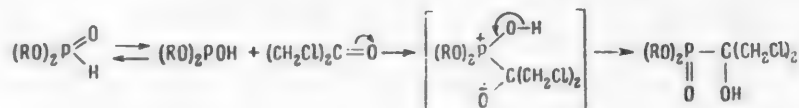
XXII. ESTERS OF α -HYDROXY- β,β -DICHLOROISOPROPYLPHOSPHINIC ACID

V. S. Abramov and A. S. Kapustina

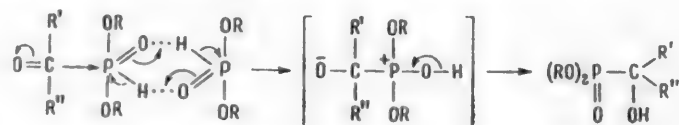
Kirov Chemico-Technological Institute, Kazan

We studied the interaction of dialkylphosphorous acids with chloroacetone [1], which led to the formation of esters of α -hydroxy- β -chloroisopropylphosphinic acid. The latter lost hydrogen chloride when treated with an alcohol solution of potassium hydroxide and were converted into esters of 1,2-epoxy-2-propylphosphinic acid. Analogous work, but for different purposes, was carried out by B. A. Arbuzov and his co-workers [2].

Extending the investigation of the interaction of dialkylphosphorous acids with halogen-substituted ketones, we studied the condensation of symmetrical dichloroacetone with dialkyl phosphites. Like certain other chloro- and nitroso-substituted carbonyl compounds [3], dichloroacetone condenses with dialkyl phosphites without a catalyst at room temperature or with gentle heating. The use of sodium alcoholate as a catalyst does not give positive results. Sodium alcoholate and the sodium dialkyl phosphite formed from it react with dichloroacetone to form sodium chloride, which complicates the reaction. The condensation of dichloroacetone occurs with the enol form of the dialkylphosphorous acid and begins between the electrophilic carbon of the carbonyl group and the lone pair of electrons of the phosphorous atom as may be represented by the scheme.



However, the tautomeric equilibrium of dialkyl phosphites is strongly displaced toward the keto-form with pentavalent phosphorous [4], therefore, for this reaction to proceed it is necessary to postulate a fast conversion into the enol form. It is probable that the condensation of aldehydes and ketones with dialkyl phosphites may also proceed with the dimer form of dialkyl phosphites [5] by the following scheme.



As a result of the condensation of dichloroacetone with dialkyl phosphites, esters of α -hydroxy- β,β -dichloroisopropylphosphinic acid were formed and these were viscous, glycerol-like liquids or crystalline substances. The properties of esters are given in Table 1.

EXPERIMENTAL

Preparation of esters of α -hydroxy- β,β -dichloroisopropylphosphinic acid. Dialkylphosphorous acids were condensed with symmetrical dichloroacetone in ampoules without catalyst. The ampoules were either kept at room temperature for a long period or heated on a boiling water bath. The condensation was considered complete

TABLE 1

Esters of α -Hydroxy- β,β' -dichloroisopropylphosphinic Acid $(RO)_2P-C(CH_2Cl)_2$
 $\begin{array}{c} \parallel \\ O \\ | \\ OH \end{array}$

Sample No.	R	Melting point	n_D^{20}	d_4^{20}	$M R_D$		Yield (in %)	% Cl		% P	
					found	calc.		found	calc.	found	calc.
1	CH ₃	57—58°	1.4790	1.4295	47.29	47.41	59.3	29.53, 29.45	29.95	12.92, 12.90	13.08
2	C ₂ H ₅	45—46	—	—	—	—	27.1	26.69, 26.78	26.80	11.48, 11.54	11.70
3	C ₃ H ₇	—	1.4670	1.2235	66.67	65.87	22.0	24.12, 23.99	24.23	10.36, 10.26	10.58
4	iso-C ₃ H ₇	79—80	—	—	—	—	69.8	24.27, 24.43	24.23	10.54, 10.52	10.58
5	C ₄ H ₉	—	1.4600	1.1711	75.28	75.12	26.0	21.70, 21.65	22.12	9.38, 9.44	9.65
6	iso-C ₄ H ₉	55—56	—	—	—	—	32.0	21.60, 21.60	22.12	9.35, 9.40	9.65

when the refractive index of the reaction mixture, which was measured periodically, remained constant. The conditions for condensing dialkylphosphorous acids with dichloroacetone are presented in Table 2.

The reaction products remained liquid. The following were obtained in a crystalline state after standing for a long time at room temperature: The diisopropyl ester of α -hydroxy- β,β' -dichloroisopropylphosphinic acid, which was recrystallized from anhydrous alcohol, and the diisobutyl ester of α -hydroxy- β,β' -dichloroisopropylphosphinic acid, which was recrystallized from aqueous alcohol. The other condensation products were purified by washing out [6].

TABLE 2

Sample No.	R in $(RO)_2POH$	Amount of reagents (in g)		Heating temperature	Heating time
		acid	dichloro-acetone		
1	CH ₃	2.7	3.2	Room	More than 4 months
2	C ₂ H ₅	46.0	42.6	} 100°	More than 30 hours
3	C ₃ H ₇	8.3	6.4		10 hours
4	iso-C ₃ H ₇	4.1	3.2	Room	More than 4 months
5	C ₄ H ₉	9.7	6.4	} 100°	10 hours
6	iso-C ₄ H ₉	9.7	6.4		

The diethyl ester of α -hydroxy- β,β' -dichloroisopropylphosphinic acid crystallized when treated with a solution of sodium chloride and it was recrystallized from cyclohexane. The yield of the crystalline substance is given. In subsequent experiments the ethyl ester was obtained directly in the crystalline state by seeding the condensation products with crystals of the ester. However, the ester crystallized slowly and with difficulty and

much of the product remained in the mother solution. The dimethyl ester of α -hydroxy- β,β' -dichloroisopropylphosphinic acid remained liquid after treatment with sodium chloride solution and purification. Its constants were determined and are given in Table 1. The ester then crystallized during work with it and it was recrystallized from cyclohexane.

The n-propyl and n-butyl esters of α -hydroxy- β,β' -dichloroisopropylphosphinic acid were purified by washing with sodium chloride solution and were successively treated with aluminum oxide and animal charcoal, but remained as sirups. When cooled below 0° , the n-propyl ester solidified to a crystalline mass which melted at $15-18^\circ$.

SUMMARY

It was shown that symmetrical dichloroacetone reacts with dialkyl phosphites without catalyst at room temperature or on heating and gives esters of α -hydroxy- β,β' -dichloroisopropylphosphinic acid.

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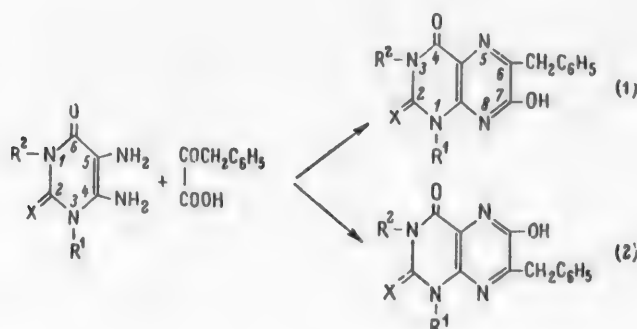
SYNTHESIS OF PTERIDINES FROM 4,5-DIAMINOPYRIMIDINES AND AROMATIC α -KETO ACIDS

II. INVESTIGATION OF REACTION BETWEEN 4,5-DIAMINOPYRIMIDINES AND PHENYLPYRUVIC ACID

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As is known from literature data [1-3], condensations of 4,5-diaminopyrimidine derivatives with unsymmetrical dicarbonyl compounds, for example, keto acids, may proceed in two directions and this leads to the formation of pteridines with isomeric structures. For example, when phenylpyruvic acid is used, the course of the reaction may be represented by the following scheme.



The direction of the reaction is determined by the behavior of the 4,5-diaminopyrimidine under the given conditions, the nature of the carbonyl reagent and the character of the medium. When 4,5-diaminopyrimidines are condensed with α -keto acids or their esters, the result of the reaction largely depends on the activity of the keto group and the acidity of the medium. Thus, for example, the reaction of aliphatic α -keto acids with 2,4,5-triamino-6-hydroxypyrimidine in a weakly acid medium forms a mixture of xanthopterin (2) and isoxanthopterin (1) derivatives, while reactions under the same conditions, but with substances in which the carbonyl group is activated by a second negative group, for example, with oxalylacetic ester and its derivatives or mesoxalic ester [4, 5], the reaction forms largely or exclusively derivatives of the isoxanthopterin series (Formula 1). When the condensation occurs in a strongly acid medium (pH 2), the reaction between α -keto acids or α -keto esters and 2,4,5-triamino-6-hydroxypyrimidine is predominantly an acylation and forms xanthopterin derivatives, i. e., the keto group in this case reacts with the NH_2 group at position 4 of the pyrimidine nucleus [4, 5].

Since the direction of the reaction between aromatic α -keto acids and 4,5-diaminopyrimidine derivatives at different pH values has not been described in the literature, it seemed interesting to study this condensation in media of different acidities. We used phenylpyruvic acid as the dicarbonyl derivative [6]. The reaction was carried out by the procedure we described previously [2] in different organic solvents (50 and 96% alcohol, glycol and isoamyl alcohol) and also in 0.01 N hydrochloric acid.

From the literature [7] it is known that the NH_2 group in position 5 of the pyrimidine nucleus is more reactive than the NH_2 group in position 4; therefore, it can be assumed that the keto group of phenylpyruvic acid, which is activated by the benzyl radical, will condense more readily with the amino group in position 5, i.e., in alcohol solutions with mineral acids absent from the medium, the condensation must lead to the formation of 7-hydroxy derivatives (Formula 1). In a condensation of 0.01 N hydrochloric acid, when the amino group in position 5 is largely in the form of the salt, the keto group of phenylpyruvic acid will react largely with the amino group in position 4, i.e., the formation of 6-hydroxy derivatives of pteridine or mixtures of these products with the 6-hydroxy isomer predominating is more probable.

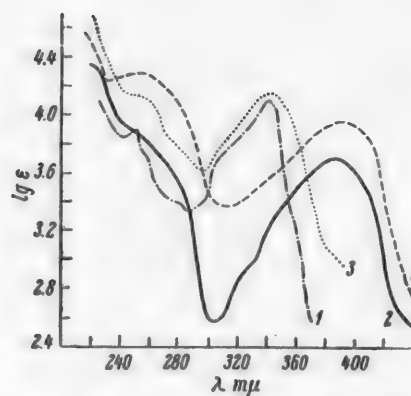


Fig. 1. Ultraviolet absorption spectra in 0.1 N NaOH solution. 1) Isoxanthopterin, 2) xanthopterin, 3) 6-benzylisoxanthopterin, 4) 7-benzylxanthopterin.

By condensation of phenylpyruvic acid with 2,4,5-triamino-6-hydroxypyrimidine in 0.01 N hydrochloric acid we obtained two substances which differed strongly from each other in properties. One of these, A, had a bright yellow color and was readily soluble in 5% hydrochloric acid, i.e., had basic properties. The main absorption band of this product and the product of its methylation lay in the region 380-390 mμ (Figs. 1 and 2), which is close to the spectrum of xanthopterin, for which the maximum lies at 395 mμ [8]. The other, almost colorless substance, B, was separated from A due to its insolubility in 5% hydrochloric acid, i.e., it had more acid properties than A. A higher acidity and light color are characteristic of isoxanthopterin derivatives. The main absorption band of this product and its methyl derivative lie in the range 341-347 mμ (Figs. 1 and 2), which almost coincides with the absorption band of isoxanthopterin (339 mμ) [9]. Substance B

should be assigned the structure of Formula 1, i.e., 2-amino-4,7-dihydroxy-6-benzylpteridine.

The substance obtained from the same starting materials but in 50% alcohol differed from A and B in properties and spectra and was found to be a mixture of these two isomers (Fig. 3). Using the method of Flördt [10], we used the spectral curves to calculate the percentage content of these isomers in the mixture and obtained

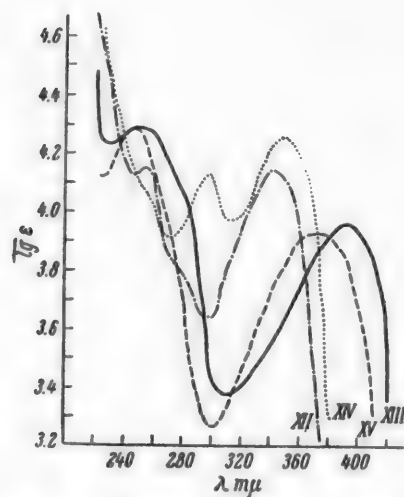


Fig. 2. Ultraviolet absorption spectra of pteridines in 0.1 N NaOH solution (XIV* in alcohol solution).

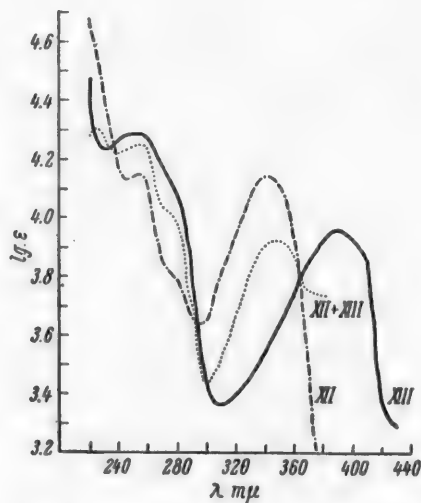


Fig. 3. Ultraviolet absorption spectra of pteridines in 0.1 N NaOH solution (mixture of XII and XIII obtained by reaction in 50% alcohol).

* Here and below the Roman numbers correspond to the numbers of the substances.

TABLE 1

Substance No.	Substituents in Formula (1)*			Yield (in %)	Melting point	Color of substance	Color of fluorescence
	R'	X	R ²				
I	o-CH ₃ C ₆ H ₄	O	H	77	328°	Colorless	Violet
II		O	CH ₃	74	318	Light yellow	
III	p-CH ₃ C ₆ H ₄	O	H	70	325	Colorless	
IV		O	CH ₃	69	182	Light yellow	
V	o-CH ₃ OC ₆ H ₄	O	H	87	330	Colorless	Blue violet
VI		O	CH ₃	65	312	The same	Violet
VII	p-(C ₂ H ₅) ₂ NC ₆ H ₄	O	H	72	192	" "	Does not fluoresce
VIII	p-CH ₃ OC ₆ H ₄	O	H	75	311	" "	Violet
IX		O	CH ₃	58	228	Light yellow	
X	p-C ₂ H ₅ OC ₆ H ₄	O	H	82	197	Light brown	Blue violet
XI		O	CH ₃	58	273	The same	Violet
XII	H	NH	H	32	441	Light sand color	Blue violet
XIII*	H	NH	H	40	320	Yellow	Greenish blue

* For XIII the substituents are in Formula (2).

TABLE 2

Substance No.	Condensation medium	Recrystallization solvent	Empirical formula of substance	% N	
				found	calc.
I*	96% alcohol	70% alcohol	C ₂₀ H ₁₈ O ₃ N ₄	15.53	15.55
II*	96% alcohol	60% alcohol	C ₂₁ H ₁₈ O ₃ N ₄	15.15	14.97
III	96% alcohol	Acetone	C ₂₀ H ₁₈ O ₃ N ₄	15.32	15.55
IV	96% alcohol	50% alcohol	C ₂₁ H ₁₈ O ₃ N ₄	14.70	14.97
V*	96% alcohol	96% alcohol	C ₂₀ H ₁₈ O ₄ N ₄	14.59	14.89
VI*	96% alcohol	96% alcohol	C ₂₁ H ₁₈ O ₄ N ₄	14.41	14.35
VII	96% alcohol	96% alcohol	C ₂₃ H ₂₃ O ₃ N ₅	16.91	16.78
VIII*	96% alcohol	96% alcohol	C ₂₀ H ₁₈ O ₄ N ₄	14.77	14.89
IX*	Isoamyl alcohol + + CH ₃ COOH	50% alcohol	C ₂₁ H ₁₈ O ₄ N ₄	14.21	14.35
X	Glycol	Isoamyl alcohol	C ₂₁ H ₁₈ O ₄ N ₄	14.58	14.35
XI*	Glycol	Isoamyl alcohol	C ₂₂ H ₂₀ O ₄ N ₄	13.40	13.86
XII	0.01 N HCl	Reprecipitation with HCl from alkali solution	C ₁₃ H ₁₁ O ₂ N ₅ · 2H ₂ O	22.97	22.94
XIII	0.01 N HCl	5% hydrochloric acid	C ₁₃ H ₁₁ O ₂ N ₅ · HCl	22.90	22.91

* These pteridines were also obtained in 0.01 N HCl.

the results of about 46% for the isoxanthopterlin derivative and 58% for the xanthopterlin derivative (the error of the method is 3-4%).

Different derivatives of 2,6-dihydroxy-4,5-diaminopyrimidine were also condensed with phenylpyruvic acid and the reaction was performed in an alcohol medium. This yielded quite homogeneous colorless or slightly colored reaction products. An examination of the absorption spectra of the pteridines obtained (Fig. 5) shows that their main absorption maximum lies in the wavelength range 330-338 m μ . The light color of the pteridines obtained indicates that they were 7-hydroxy derivatives (Formula 1) as the 6-hydroxy isomers of pteridine (Formula 2) usually have an intense color. Therefore, it can be assumed that the compounds we obtained under these conditions were 7-hydroxy derivatives of pteridine, which completely agrees with literature data [11] and theoretical ideas. It is evident that under these conditions the reaction leads to the formation of 7-hydroxy isomers.

The pteridines obtained and some of their properties are given in Tables 1 and 2.

All the pteridines obtained dissolved in alkalis and some organic solvents (pteridine VII was also soluble in mineral acids). With the exception of the solution of (VII), the alkaline solutions showed fluorescence in ultraviolet light. The compounds were all capable of forming mono- and disubstituted salts of the heavy metals Ag, Pb and Cu, which were difficultly soluble in water and alcohol, and pteridine (IX) also formed a difficultly soluble sodium salt. The action of dimethyl sulfate on alkaline solutions of the pteridines formed the N-methyl derivatives. Thus, methylation of pteridine (V) yielded (VI), (VIII) gave (IX), (II) yielded 1-o-tolyl-3,8-dimethyl-2,4,7-trioxopteridine and (III) yielded 1-p-tolyl-3,8-dimethyl-2,4,7-trioxopteridine. Methylation of pteridine (XII) in alkaline solution with dimethyl sulfate gave a methylation product with a yellow color, namely, 1,3,8-trimethyl-2-imino-4,7-dioxo-6-benzylpteridine, and methylation of (XIII) yielded its dimethyl derivative. The pteridines were brominated to form monobromo derivatives by the action of bromine in glacial acetic acid. Under these conditions we obtained a monobromo derivative of pteridine (VIII) and also 1,3-dimethyl-2,4-dioxo-7-hydroxy-6-benzylpteridine, which we described previously [2].

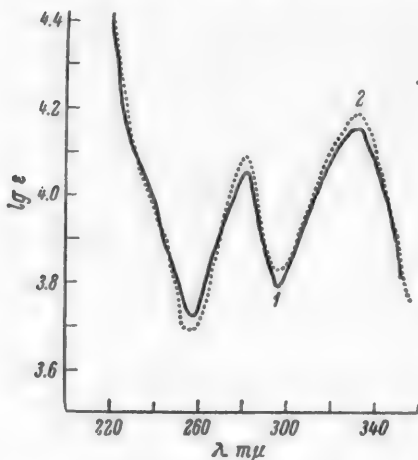


Fig. 4. Ultraviolet absorption spectra of pteridine (VI), obtained in 95% alcohol (1) and in 0.01 N HCl (2) (solutions in 0.1 N NaOH).

EXPERIMENTAL

2-Amino-4,7-dihydroxy-6-benzylpteridine (XII) and 2-amino-4,6-dihydroxy-7-benzylpteridine (XIII) and their methylation products. 2.57 g (0.01 mole) of 2,4,5-triamino-6-hydroxypyrimidine sulfate was heated to boiling in 300 ml of 0.01

N HCl and 1.64 g (0.01 mole) of phenylpyruvic acid added to the reaction mixture. The mixture was boiled for 6 hours. The reaction components first gradually dissolved and then the solution became turbid and a precipitate formed. After the mixture had been cooled, the precipitate was collected, dissolved in 5% NaOH and reprecipitated with CH₃COOH. The precipitate was dissolved again in NaOH and the alkaline solution of the pteridine added dropwise to boiling 5% hydrochloric acid. The insoluble part was collected and purified by boiling with 5% HCl twice and washing with hot water. The substance obtained had a light sandy color, dissolved readily in alkalis, but was insoluble in organic solvents and had m. p. 441° (on a Maquenne block). An alkaline solution of this substance had a blue-violet fluorescence. The product contained 2 molecules of bound water, which could not be removed at 100°. The yield was 0.95 g. Judging by the ultraviolet absorption curve presented (Fig. 2), the substance was a derivative of isoxanthopterlin, i. e., it was 2-amino-4,7-dihydroxy-6-benzylpteridine (XII).

Found %: N 22.97. C₁₃H₁₁O₂N₅ · 2H₂O. Calculated %: N 22.91.

The remaining hydrochloric acid solution after separation of (XII) was evaporated to small volume (about 70-80 ml) and cooled. An intense yellow substance separated and this was recrystallized several times from 5% hydrochloric acid. The m. p. was 320° (on a Maquenne block). The yield was 1.2 g. An alkaline solution of the pteridine had a very intense greenish-blue fluorescence. The substance contained HCl in its composition and was the hydrochloride of 2-amino-4,6-dihydroxy-7-benzylpteridine (XIII), whose absorption maximum in the ultraviolet corresponded to the absorption maximum of xanthopterlin (Fig. 1).

Found %: N 22.90. $C_{15}H_{12}O_2N_5Cl$. Calculated %: N 22.91

The action of dimethyl sulfate on an alkaline solution of (XII) formed a yellow substance, which was insoluble in alkalis and was 1,3,8-trimethyl-2-imino-4,7-dioxopterin (XIV). After recrystallization from alcohol, the substance had m. p. 237.5°. The alcohol solution had a very strong blue-violet fluorescence.

Found %: N 22.35. $C_{16}H_{17}O_2N_5$. Calculated %: N 22.50.

Methylation of (XIII) formed a yellow substance which dissolved in solutions of NaOH and ammonia and was the dimethyl derivative (XV). The m. p. was 415° (with decomp.). An alkaline solution of (XV) had an intense blue fluorescence.

Found %: N 23.29. $C_{15}H_{15}O_2N_5$. Calculated %: N 23.56.

Phenylpyruvic acid was also reacted with 2,4,5-triamino-6-hydroxypyrimidine sulfate in 50% alcohol. We had mistakenly taken the substance formed (m. p. 340°) as homogeneous [2], but in actual fact it was a mixture of isomers (XII) and (XIII) and was separated into the corresponding components by the action of hot HCl. We used Firordt's method to determine the composition of this mixture; the values of the absorption of the separate components at a definite wavelength and the absorption of the mixture at the same wavelength were used for the calculation. The calculations showed that there was about 46% of isomer (XII) in the mixture and about 58% of isomer (XIII) ($\pm 4\%$).

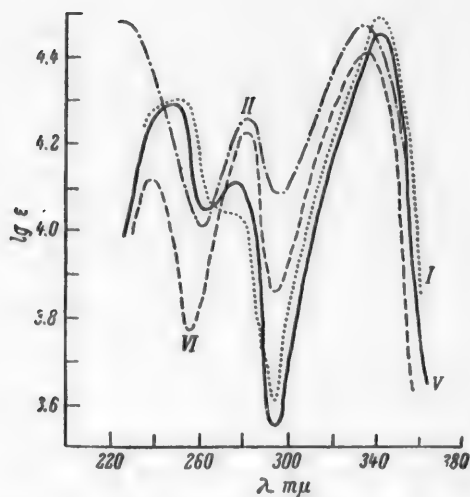


Fig. 5. Ultraviolet absorption spectra of pteridines in 0.1 N NaOH.

1-o-Tolyl-2-oxo-4,7-dihydroxy-6-benzylpteridine (I) and pteridines (II-XI). A solution of 2.32 g (0.01 mole of

3-o-tolyl-4,5-diaminouracil and 1.64 g (0.1 mole) of phenylpyruvic acid in 100 ml of alcohol was boiled for a long period. At the end of the reaction (free acid and uracil were absent from the solution), the alcohol was removed by distillation and the solid residue dissolved in 5% NaOH, reprecipitated with 5% hydrochloric acid and recrystallized from 70% alcohol. The m. p. was 328°. The yield was 2.77 g. The alkaline solution had an intense violet fluorescence in ultraviolet light.

Found %: N 15.53. $C_{20}H_{16}O_3N_4$. Calculated N 15.55.

The pteridines (II-XI) were obtained analogously from phenylpyruvic acid and the corresponding 4,5-diaminouracils.

Phenylpyruvic acid was condensed with 2,6-dihydroxy-4,5-diaminopyrimidines in 0.01 N HCl by boiling equimolecular amounts of the starting materials. As an example we describe the synthesis of pteridine (I). 1.16 g (0.005 mole) of 3-o-tolyl-4,5-diaminouracil was heated to boiling with 50 ml of 0.01 N hydrochloric acid and to the reaction mixture was added 0.82 g (0.005 mole) of phenylpyruvic acid. As the initially formed solution was boiled, a precipitate formed. Boiling lasted for about 30 minutes. The precipitate was reprecipitated from 5% NaOH with hydrochloric acid and recrystallized from 70% alcohol. The m. p. was 328°. The absorption spectrum of the compound obtained agreed completely with that of pteridine (I). From the identity of physical properties (solubility, melting point, absorption spectra and fluorescence color) and also the chemical properties (same acidity and the capacity to form identical salts) we consider that the products obtained in an alcohol medium and in 0.01 N HCl are identical.

Similarly, reaction in 0.01 N HCl was used to obtain pteridines (II), (V), (VI), (VIII), (IX) and (XI) and also pteridines that we had described previously [2], 2,4,7-trioxo-6-benzylpteridine, 1-phenyl-2,4,7-trioxo-6-benzyl- and 1-phenyl-3-methyl-2,4,7-trioxo-6-benzylpteridine, which were found to be identical with the corresponding pteridines obtained in alcohol.

The action of bromine on a solution of (VIII) in glacial acetic acid yielded a yellow precipitate. After recrystallization from acetone, the substance had m. p. 344°. An alkaline solution of the bromopteridine had a more intense violet fluorescence than the original pteridine.

Found %: N 12.14. $C_{20}H_{15}O_4N_4Br$. Calculated %: N 12.30.

The bromoderivative of 1,3-dimethyl-2,4-dioxo-7-hydroxy-6-benzylpteridine was obtained under the same conditions. After recrystallization from 60% alcohol, the substance had m. p. 320° (with decomp.).

Found %: N 14.87. $C_{15}H_{13}N_4Br$. Calculated %: N 14.85.

The ultraviolet absorption spectra of the pteridines obtained were plotted on an SF-4 photoelectric spectrophotometer.* The solutions for plotting the spectra contained 0.01 g of pteridine in 1000 ml of 0.1 N NaOH; the cell thickness was 1 cm. The characteristic absorption bands and the corresponding molecular extinction coefficients are presented in Table 3, and the absorption curves of some pteridines are given in Figs. 2, 4 and 5.

TABLE 3

Substance No.	λ_{\max} (in m μ)	lg ϵ	λ_{\min} (in m μ)	lg ϵ
I	250, 338	4.28, 4.39	290	3.57
II	280, 333	4.16, 4.38	234, 295	4.16, 3.74
III	251, 338	4.28, 4.40	235, 295	4.14, 3.75
IV	309	4.27	261	3.88
V	245, 275, 338	4.23, 4.05, 4.38	261, 295	3.99, 3.51
VI	281, 332	4.08, 4.18	255, 295	3.68, 3.82
VII	256, 336	4.25, 4.19	235, 295	4.15, 3.78
VIII	250, 275, 338	4.39, 4.20, 4.34	235, 295	4.21, 3.81
IX	280, 330	3.97, 4.06	261, 295	3.66, 3.74
X	274, 335	4.10, 3.67	261, 315	3.84, 3.53
XI	280, 332	3.96, 4.07	261, 295	3.79, 3.83
XII	255, 341	4.15, 4.15	247, 295	4.13, 3.64
XIII	253, 391	4.29, 3.96	231, 315	4.23, 3.38
XIV**	218, 296, 347	4.76, 4.13, 4.26	270, 310	3.91, 3.97
XV	244, 370	4.28, 3.93	225, 313	4.11, 3.26

* The spectrum was plotted in alcohol solution.

The data in Table 3 and Fig. 5 indicate that the introduction of a methyl group into position 3 has a considerable effect on the absorption spectra, that is especially strong in the region 240-280 m μ , which, as is known [12], corresponds to the absorption region of the pyrimidine nucleus. The change in electron density produced by the methyl group leads to a hypsochromic shift in the absorption band at 240 m μ by 10-20 m μ and in the band at 340 m μ , by 5-8 m μ and a bathochromic shift in the absorption maximum at 280 m μ by 4-5 m μ .

SUMMARY

1. By condensation of 2,4,5-triamino-6-hydroxypyrimidine with phenylpyruvic acid in 0.01 N HCl (pH 2) we obtained the two possible isomers, 6-benzylisoxanthopterin and 7-benzylxanthopterin, and identified them; their methyl derivatives were obtained by methylation with dimethyl sulfate.

Condensation of the same components in 50% alcohol also formed a mixture of the two isomers.

2. Condensation of 2,6-dihydroxy-4,5-diaminopyrimidine derivatives with phenylpyruvic acid in alcohol yielded 11 new pteridine derivatives. Here the reaction led to the formation of 7-hydroxy derivatives. Similar products were obtained by condensation in 0.01 N hydrochloric acid.

3. Some methylation and bromination products were obtained from the pteridines synthesized.

4. The ultraviolet spectra of the products obtained were plotted and the effect of methyl groups in position 3 on the shift in the absorption bands was established.

*The spectra were plotted by T. N. Gladyshevskaya.

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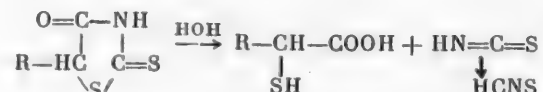
SYNTHESIS AND CONVERSIONS OF SOME THIAZOLIDINE DERIVATIVES

III. HYDROLYSIS OF AZORHODANINES

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A characteristic property of thiazolidines is their capacity for alkaline hydrolysis with ring opening. Rhodanine and its derivatives which are not substituted at the nitrogen atom are hydrolyzed when heated with alkalis to form α -mercaptocarboxylic and isothiocyanic acids and the latter then isomerizes into thiocyanic acid.

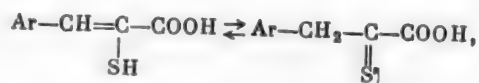


The strength of the thiazolidine ring in rhodanine and its derivatives in relation to the substituents has been studied by N. M. Turkevich and his co-workers. Thus, it was shown [1] that unsubstituted rhodanine cannot be precipitated from alkalis, since it is hydrolyzed by the above scheme not only on heating, but even in the cold. The presence of a substituent in position 5, for example, a methyl group, leads to strengthening of the thiazolidine ring [2]; the latter is particularly stabilized by the introduction of an aldehyde residue into the rhodanine molecule. Thus, 5-benzylidenerhodanine can even be sulfonated with strong H_2SO_4 at 110° [3], while boiling with alkalis is required for qualitative detection of its hydrolysis products. The hydrolysis of 5-arylidene derivatives of rhodanine was investigated by Andreasch [4], Zipser [5], and others. Turkevich and Shvydkii [6], who studied the kinetics of alkaline hydrolysis, showed on the example of rhodanine and 5-methylrhodanine that the hydrolysis of rhodanines is a second order reaction. Alkaline hydrolysis of N-substituted rhodanines is much more complex and the primary hydrolysis products are thioglycolic acids and mustard oils, which are then hydrolyzed further to form amines, sulfides and carbonates.

Some mustard oils are converted into thioureas by hydrolysis. Andreasch and Zipser [7] showed that the alkaline hydrolysis of N-phenylrhodanine yielded thioglycolic acid and also CO_2 , SO_2 and diphenylthiourea.

On the basis of an investigation of the alkaline hydrolysis products of thiazolidines, Turkevich and Makukha [8] proposed a method for the qualitative analysis of rhodanines, thiazolidinediones, pseudothiohydantoins etc., which makes it possible to determine the character of preparations of the thiazolidine series of undetermined structure.

α -Mercaptocarboxylic acids, which can be obtained by alkaline hydrolysis of 5-arylidenerhodanines, are of great practical interest. As they are in tautomeric equilibrium with thioketo acids

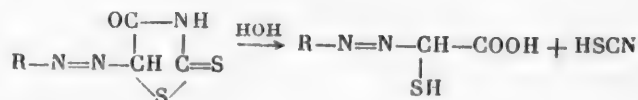


they are capable of forming oximes, hydrazones etc., which make it possible to synthesize complex α -amino acids which are difficultly accessible by other methods. The condensation of α -thioketo acids with pyrimidines is

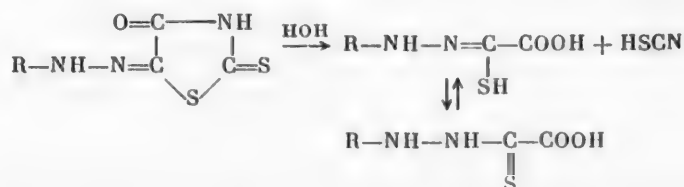
used for the synthesis of pteridines [9, 12]. Rhodanine and its derivatives also undergo (but with much more difficulty) acid hydrolysis, but this has been studied little due to its small practical importance. Thus, Klason [10] obtained thioglycolic acid and thiazolidinedione-2,4 by hydrolysis of rhodanine with hydrochloric acid at 130°.

We set out to study the alkaline hydrolysis of azorhodanines, the products of coupling rhodanine with diazonium salts, which we obtained for the first time [11]. As azorhodanines are 5-aryldiazoderivatives of rhodanine, it was to be expected that they would be hydrolyzed similarly to other 5-substituted derivatives, i. e., with ring rupture and the formation of 5-arylazomercaptocarboxylic acids. If we consider tautomerism of the two possible forms of azorhodanines, azo and hydrazone forms, then the hydrolysis may be represented by the two schemes:

a) for the azo form



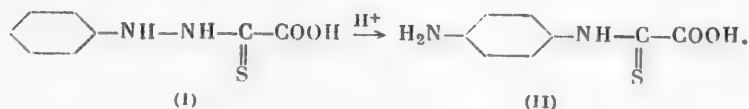
b) for the hydrazone form



We have already shown [11] that the hydrazone structure is preferable for azorhodanines. Thus, for example, a small amount of phenylhydrazine is formed when 5-phenylazorhodanine is boiled with a mixture of acetic and hydrochloric acids. An investigation of the alkaline hydrolysis products completely confirmed the fact that the reaction proceeded by Scheme "b", which is possible only if azorhodanines have a hydrazone structure.

For hydrolysis, the azorhodanine was boiled for 4-6 hours with 10-15% aqueous NaOH solution until the very characteristic intense red color disappeared. The hydrolyzate was decolorized with charcoal, cooled and acidified with dilute acid. This usually liberated a certain amount of H₂S and immediately precipitated a pale yellow precipitate, which was rapidly collected. By this method we hydrolyzed azorhodanines with aniline, p-toluidine, sulfanilamide, sulfacyl and anthranilic, p-aminobenzoic and methanilic acid residues. In all cases we obtained precipitates which were readily soluble in alcohol and very readily soluble in alkalis, indicating their acidic nature. All the substances were tested for the presence of an SH group with sodium nitroprusside and for reaction with FeCl₃ and NH₄OH, with which thioketo acids give an intense emerald green color under these conditions [1, 9]. No mercapto compounds were found in any case, though the presence of a thioketo group was demonstrated qualitatively and we also isolated crystalline precipitates of difficultly soluble iron-ammonium complexes, causing the green color. Thus, the main hydrolysis products were thioketo compounds which are apparently more stable and not isomerized into mercapto compounds. The hydrolyzates always contained a considerable amount of thiocyanic acid, indicating rupture of the thiazolidine ring.

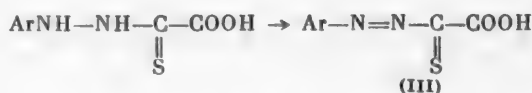
Our experiments showed that the precipitates liberated by acidification of the hydrolyzate with mineral acids (H₂SO₄ and HCl) were predominantly the amino compounds (II), formed by the action of acids on the hydrazo compounds (I), which are very prone to this rearrangement, according to the scheme



This reaction is analogous to the benzidine rearrangement and proceeds very readily when the para and ortho positions are free. Compounds (II), which are the aminoarylamides of thiooxalic acid, dissolved in

concentrated acids, formed Schiff's bases with aldehydes and could be diazotized and coupled to form azo dyes. They changed little on prolonged storage.

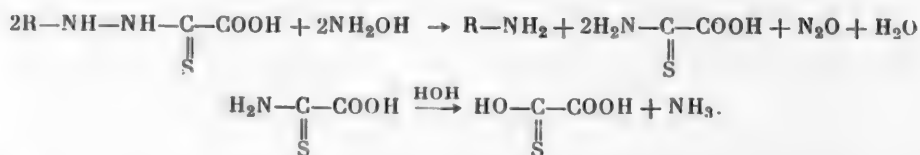
Wishing to isolate the unchanged hydrazo compounds, which are the primary and most interesting hydrolysis products, in two cases we acidified the hydrolyzate with acetic acid and saturated it with sodium chloride. Due to the low acidity of the medium, the sodium salts of the hydrazothio keto acids were isolated as pale yellow, extremely unstable, crystalline substances, which were readily oxidized to azo dyes (III) when stored in air. Alkaline solutions of the hydrazo keto acids were especially readily oxidized in the presence of iron salts, when the upper layer of the solution acquired an intense red color. This phenomenon often made it difficult to control the course of the hydrolysis



The same azo dye was obtained by oxidation of the hydrazo compound with an alkaline solution of bromine. Pyrolysis of the unpurified product from the hydrolysis of phenylazorhodanine yielded the original amine, i. e., aniline and this is characteristic of hydrazo compounds.



Reduction of the hydrazothio keto acids to the original amine was observed only when tin and hydrochloric acid were used; zinc in alkali solutions did not reduce them, i. e., our hydrazo compounds behaved similarly to hydrazobenzene. Apart from the formation of a complex salt mentioned above, the presence of a >CS group in the hydrolysis products was also demonstrated by reduction with hydrosulfite and tin in an acid medium to form mercapto compounds, which were rapidly oxidized. Interaction with hydroxylamine and semicarbazide did not give the desired derivatives, but in the case of hydroxylamine, aniline and ammonia were formed, i. e., reduction occurred according to the reaction:



Consequently, the >CS group in the substances obtained did not have characteristic thio ketone properties and compounds (I) should be regarded as arylhydrazides of thiooxalic acid.

EXPERIMENTAL

1. Acid hydrolysis of phenylazorhodanine. 7 g of purified azorhodanine was dissolved in a mixture of 70 ml of acetic acid, 80 ml of hydrochloric acid, 100 ml of dioxane and 30 ml of water. The homogeneous solution obtained was boiled for 7 hours, while it darkened and H_2S was evolved. Then $\frac{2}{3}$ of the total volume of the solution was evaporated, the residue neutralized with solid alkali and extracted with ether and the ether distilled from the extract. The small residual oily layer contained phenylhydrazine and its oxidation products, as was shown by qualitative reactions.

2. Alkaline hydrolysis of phenylazorhodanine. a) p-Aminophenylamide of thiooxalic acid (IV). 12.5 g of phenylazorhodanine was dissolved in 150 ml of 10% aqueous NaOH solution and boiled for 4 hours in a flask with a reflux condenser. The initial intense red color disappeared and after being boiled with charcoal and filtered, the solution became clear and slightly orange-yellow. H_2SO_4 (1:2.5) was gradually added to the solution with strong cooling. The solution became straw yellow and then a voluminous, golden yellow, coarsely crystalline precipitate formed. The yield was 7.5 g (71.4%). A small amount of H_2S was liberated simultaneously and a very strong and unpleasant smell was emitted. The precipitate was collected and a solution of FeCl_3 gradually added to the filtrate, when the green complex salt of the thio keto acid precipitated first and then the more soluble iron thiocyanate formed. After recrystallization from alcohol, the precipitate appeared as fine, diamond shaped

platelets with decomp. p. 205-210°, which were readily soluble in alkalis, water and alcohol and insoluble in benzene and ether. Aqueous solutions of the preparation gave precipitates (predominantly yellow) with mercury, nickel, lead, barium and silver salts. The substances dissolved in conc. H_2SO_4 with a slight coloration.

Found %: N 14.27. $\text{C}_9\text{H}_9\text{O}_2\text{N}_2\text{S}$. Calculated %: N 13.74.

It should be noted that a decrease in the alkali or azorhodanine concentration, a decrease in the heating time and also insufficient cooling during acidification could lead to the formation of only an oily substance.

With formalin, an aqueous solution of amine (IV) gradually formed (especially in an acid medium) a light yellow, lumpy precipitate of a Schiff's base (V), which did not contain amino groups. It was soluble in boiling water and readily soluble in hot alcohol and acetone. It had a characteristic smell. The substance crystallized from aqueous alcohol as fine crystals with m. p. 145.2°.

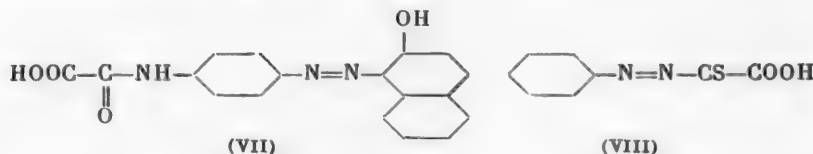
Found %: N 13.77. $\text{C}_9\text{H}_9\text{O}_2\text{N}_2\text{S}$. Calculated %: N 13.46.

Similarly, a solution of preparation (IV) gave the ethylidene derivative (VI) with acetaldehyde. The substance crystallized from aqueous alcohol as fine, yellow, odorless crystals with m. p. 135-136°.

Found %: N 12.63. $\text{C}_{10}\text{H}_{10}\text{O}_2\text{N}_2\text{S}$. Calculated %: N 12.60.

Diazotization of (IV) and subsequent coupling with an alkaline solution of β -naphthol gave a voluminous red azo dye (VII), which did not contain sulfur, apparently as a result of its oxidation by nitrous acid. The substance formed long needles on precipitation from alcohol with water in the presence of HCl.

Found %: N 12.74. $\text{C}_{18}\text{H}_{15}\text{O}_4\text{N}_3$. Calculated %: N 12.53.



Oxidation with bromine. 1 g of the crude hydrolysis product (of phenylazorhodanine) was dissolved in NaOH solution and an alkaline solution of bromine added to it with cooling in ice, when a red-brown coloration appeared. After half an hour the solution was acidified with HCl to form a green precipitate of the azo dye (VIII) (0.4 g).

The addition of formalin to the filtrate (after removal of the dye) gave a yellow precipitate of the Schiff's base (V). The dye (VIII) was insoluble in water, readily soluble in alcohol and acetic acid and less so in acetone. It decomposed at 145°. It was reduced to aniline. Alkaline solutions had a red-brown color. Purification of the preparation was difficult.

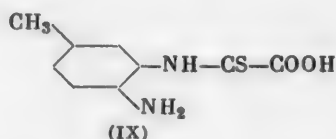
Pyrolysis. 1 g of dry, unpurified hydrolysis product of phenylazorhodanine was decomposed thermally to yield a large amount of H_2S and 0.25 g of a light yellow, water-insoluble liquid, which contained aniline as was demonstrated by a series of reactions. Phenylhydrazine and other amines were not detected.

b) Phenylhydrazide of thiooxalic acid (Na salt). An alkaline hydrolyzate, obtained as in case "a", was cooled and acidified with acetic acid (1:1). The small amount of precipitate was collected and sodium chloride added to the filtrate to produce a voluminous precipitate of the Na salt of the hydrazo compound. Two recrystallizations from 96% alcohol gave elongated yellow plates, which charred at 215-218° without melting. They were very readily soluble in water. The flame coloration and also a precipitate with $\text{K}_2\text{H}_2\text{Sb}_2\text{O}_7$ indicated the presence of sodium. The substance did not form a Schiff's base, but when it was acidified, all the properties of amino compound (IV) appeared. When the dry preparation was stored for 30-40 days, it was completely oxidized and converted into the green azo dye (VIII) mentioned above.

Found %: N 12.64. $\text{C}_8\text{H}_7\text{O}_2\text{N}_2\text{SNa}$. Calculated %: N 12.83.

3. Alkaline hydrolysis of p-tolylazorhodanine. a) 0.75 g of the azorhodanine recrystallized from nitrobenzene was dissolved in 40 ml of 6% NaOH and the solution boiled gently for 2 hours. The hydrolyzate had a

slight color, but became almost colorless after the addition of charcoal. Cooling and acidification with 20% H_2SO_4 immediately gave a precipitate of light yellow, rectangular crystals. The yield was 0.4 g (67%). No evolution of SO_2 or H_2S was observed. Recrystallization from alcohol gave long platelets with m. p. 181-189°. The preparation could be diazotized and gave a Schiff's base and was consequently the amino compound with structure (IX).



Found %: N 13.12. M (by Rast's method) 215. $C_9H_{10}O_2N_2S$. Calculated %: N 13.32. M 210.

b) 12.5 g of azorhodanine was hydrolyzed for 4 hours in 300 ml of 10% NaOH and acidified with acetic acid to give about 10 g of a voluminous, light yellow, flaky precipitate, but on storage, the latter was oxidized completely to form a brown-red substance with the properties of an azo compound. So far it has not been possible to isolate the hydrazo compound in a pure state.

4. Alkaline hydrolysis of 5-(o-carboxyphenylazo)-rhodanine. 7 g of the azorhodanine was boiled for 4 hours in 200 ml of 8% NaOH and then acidified with H_2SO_4 (1:2.5) to give 3.5 g of a creamy yellow, finely crystalline precipitate. The product was insoluble in water, but soluble in hot alcohol, acetic acid and dioxane. Reprecipitation from NaOH with hydrochloric acid and then from dioxane with water yielded fine light yellow crystals, which gave positive reactions for C-COOH and NH_2 groups and also showed some properties of a hydrazo compound.



The hydrolysis product evidently contained two isomeric substances.

Found %: N 11.36. $C_9H_8O_4N_2S$. Calculated %: N 11.61.

SUMMARY

1. Acid and especially alkaline hydrolysis of azorhodanines confirmed their hydrazone structure.
2. The main primary products of alkaline hydrolysis of azorhodanines were the previously unknown hydrazothio keto compounds, arylhydrazides of thiooxalic acid, and also thiocyanic acid. Mercapto compounds were not formed.
3. Hydrazothio keto acids are extremely unstable and under the action of hydrogen ions, they readily undergo a rearrangement similar to the benzidine rearrangement to give the corresponding amino compounds, aminoaryl-amides of thiooxalic acid. They are readily oxidized to azo compounds.
4. The $>CS$ group in the hydrolysis products obtained did not possess characteristic thio ketone properties and did not give corresponding derivatives.

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INTERACTION OF PIPERYLENE α -OXIDES WITH HYDROGEN CHLORIDE

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We recently prepared the isomeric α -oxides of piperylene [1] but their chemical properties have not been studied sufficiently as yet. The piperylene α -oxides were reacted with water, acetic anhydride, acetyl chloride, and ethyl alcohol [2]. Descriptions were recently given of the isomerization and hydration of piperylene α -oxide (3,4-oxidopentene-1) and also its interaction with acetone, methanol and diethylamine [3].

In continuing and developing the investigations we began, we studied the addition of hydrogen chloride to 3,4-oxidopentene-1 and established the course of opening of the oxide ring in this reaction. Experiments were also carried out on the interaction of hydrogen chloride and hydrochloric acid with the isomeric oxide, 1,2-oxidopentene-3, which did not lead to positive results.

A. A. Petrov [4] and Kadesch [5] established that the addition of hydrohalic acids to butadiene α -oxide proceeds contrary to Markovnikov's rule to form chlorohydrins, isomeric with the chlorohydrins obtained by the action of hypochlorous acid on butadiene. Due to the absence of a sharp difference in the effect of the substituent groups in 3,4-oxidopentene-1 on the polarization of the oxide molecule, in our case one might expect the interaction of the oxide with hydrogen chloride to form 4-chloropenten-1-ol-3, 3-chloropenten-1-ol-4 or a mixture of them.

As a result of the reaction of 3,4-oxidopentene-1 with dilute hydrochloric acid, we obtained only one product, which was a monochlorohydrin of piperylene, as was confirmed by analysis data on the chlorine content and calculation of the molecular refraction.

For proving the structure of unsaturated chlorohydrins, Kadesch [5] and A. N. Pudovik and B. E. Ivanov [2] studied the rate of their hydrolysis in aqueous solutions. It was established that only chlorohydrins with the chlorine atom in the allyl position were hydrolyzed readily. Our study of the rate of hydrolysis of the chlorohydrin obtained in 0.1 M aqueous solution at 70° showed that the chlorohydrin was 90% hydrolyzed after 3 hours. When the chlorine atom is isolated from the double bond in the chlorohydrin, the hydrolysis rate is less by a considerable factor: According to available data, under these conditions such chlorohydrins are 3-7% hydrolyzed. The ease of hydrolysis indicated that the chlorine atom in the chlorohydrin obtained was in the allyl position, i. e., the compound had the structure $\text{CH}_2=\text{CHOH}-\text{CHCl}-\text{CH}=\text{CH}_2$.

The presence of the double bond was established by bromination of the chlorohydrin. We obtained 1,2-dibromo-3-chloropentanol-4 in 80% yield. Oxidation of this with chromic mixture in glacial acetic acid formed 1,2-dibromo-3-chloropentanone-4 in 80% yield.

The interaction of 1,2-oxidopentene-3 with dry hydrogen chloride in solvents or with hydrochloric acid was accompanied by tar formation and it was impossible to isolate any reaction products from experiments under various conditions.

EXPERIMENTAL

Addition of hydrogen chloride to 3,4-oxidopentene-1. 28 g of 3,4-oxidopentene-1 was added dropwise to 75 ml of 25% hydrochloric acid. The reaction proceeded with the evolution of heat. The reaction mixture was cooled (15-16°) then stirred for 1 hour and finally extracted 5 times with ether. The ether solution was dried

with calcium chloride, the ether removed and the residue distilled at 13 mm with a Widmer fractionating column. We obtained about 2 g of a fraction with b. p. up to 49°, 27 g of product with b. p. 49-51° and 2 g of residue. Redistillation of the fraction 49-51° at 13 mm gave 25 g of 3-chloropenten-1-ol-4.

B. p. 49-50° (13 mm), n_D^{20} 1.4600, d_4^{20} 1.0544, MR_D 31.48; Calc. 31.25.

Found %: Cl 29.52. C_5H_9OCl . Calculated %: Cl 29.46.

Bromination of 3-chloropenten-1-ol-4. A solution of 43 g of bromine in 35 ml of chloroform was added dropwise with cooling (0°) to 26 g of 3-chloropenten-1-ol-4 in 20 ml of chloroform. The chloroform was removed and the residue vacuum distilled. We obtained 45 g of 1,2-dibromo-3-chloropentanol-4.

B. p. 137-139° (15 mm), n_D^{20} 1.5500.

Found %: Cl+2Br 70.27. $C_5H_9OClBr_2$. Calculated %: Cl+Br 69.70.

1,2-Dibromo-3-chloropentanol-4 was a very viscous liquid without smell or color, which became yellow when stored. It was soluble in ether, alcohol and chloroform.

Oxidation of 1,2-dibromo-3-chloropentanol-4 with sodium bichromate. With vigorous mechanical stirring, 17 g of 96% sulfuric acid was added dropwise to a solution of 22.4 g of sodium bichromate and 45 g of 1,2-dibromo-3-chloropentanol-4 in 100 ml of glacial acetic acid. The reaction mixture was stirred vigorously and cooled (15-17°) for 3 hours. The reaction mixture was then diluted with water and washed twice with ether. The ether solution of 1,2-dibromo-3-chloropentanol-4-one was washed several times with 10% sodium carbonate solution and dried over calcium chloride, the ether removed by distillation on a water bath and the residue vacuum distilled from an Arbuzov flask. After a second distillation with a Widmer column, 20 g of 1,2-dibromo-3-chloropentanol-4-one was isolated.

B. p. 115-116° (15 mm), n_D^{20} 1.5382, d_4^{20} 1.8985, MR_D 45.90; Calc. 44.69.

Found %: Cl+2Br 69.46. $C_5H_7OClBr_2$. Calculated %: Cl+2Br 70.20.

1,2-Dibromo-3-chloropentanol-4-one was a mobile liquid, which rapidly became yellow and then darkened in light. It was soluble in ether, alcohol and chloroform, but insoluble in water. It was strongly lachrymatory.

Hydrolysis rate of piperylene chlorohydrin. Portions of 1.205 g each of chlorohydrin were weighed into three 100 ml measuring flasks. The flasks were filled to the mark with water at 70°, shaken until the samples dissolved completely and placed in a thermostat at $70 \pm 0.3^\circ$. The concentration of Cl^- in samples taken was determined by titration according to the Volhard method. ($AgNO_3$ 0.001717; 10 ml of $AgNO_3$ was equivalent to 10.1 ml of NH_4CNS). The data are presented in the table.

Time (in minutes)	$AgNO_3$ taken (in ml)	NH_4CNS consumed in titration (in ml)			Chlorohydrin hydrolyzed (in%)		
		I 4	II 4	III 4	I 4	II 4	III 4
0	10	10.1	10.1	10.1	0	0	9
30	10	5.0	5.1	4.95	50.50	49.51	51.00
60	10	—	3.2	3.1	—	68.32	70.30
90	10	2.2	2.2	2.1	78.22	78.22	79.21
120	10	1.5	1.6	1.5	85.15	84.16	85.15
150	10	1.1	1.2	1.1	89.11	88.12	89.11
180	10	1	—	—	90.10	—	—

Addition of hydrogen chloride to 1,2-oxidopentene-3. With cooling in ice, 25 g of 1,2-oxidopentene-3 was added dropwise to 75 ml of 25% hydrochloric acid. The addition of each drop produced strong heating in the reaction mixture. The formation of a considerable amount of tar was observed and it was impossible to isolate any reaction products. Reactions with more concentrated (31%) and less concentrated (15%) hydrochloric acid did not give positive results either.

A stream of dry hydrogen chloride was passed through 25 ml of 1,2-oxidopentene-3 with cooling in ice until the increase in weight was 7.3 g. During vacuum distillation of the reaction mixture, which was a dark,

viscous liquid, tar formation occurred and it was impossible to isolate reaction products.

Reactions with ether solutions of 1,2-oxidopentene-3 did not give positive results.

SUMMARY

1. The interaction of 3,4-oxidopentene-1 and 1,2-oxidopentene-3 with hydrochloric acid and hydrogen chloride was studied.

2. It was shown that the main product formed by the addition of hydrogen chloride to 3,4-oxidopentene-1 was 3-chloropenten-1-ol-4.

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NEW METHOD OF SYNTHESIZING ESTERS OF PHOSPHINIC AND THIOPHOSPHINIC ACIDS

XXXI. ADDITION OF PHOSPHOROUS AND HYPOPHOSPHOROUS ACIDS, DIALKYLPHOSPHOROUS ACIDS AND PHOSPHONOACETIC ESTERS TO MALEIC ESTERS

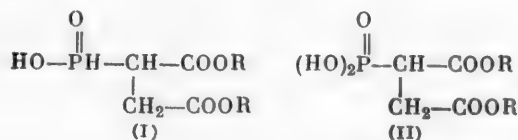
A. N. Pudovik, T. M. Moshkina, and I. V. Konovalova

Kazan Branch of the Motion Picture Scientific Research Institute

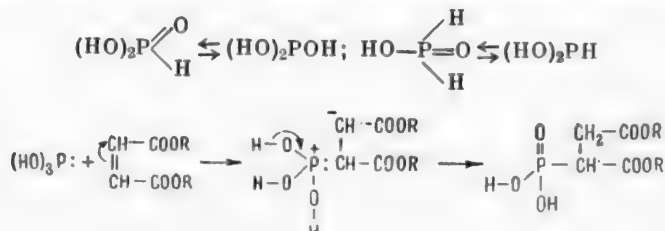
In previous work we showed that partial esters of phosphorous, thiophosphorous and phosphinous acids of the general form



add readily in the presence of alkaline catalysts to unsaturated compounds of the electrophilic type: Esters of unsaturated monobasic and dibasic carboxylic acids, unsaturated nitriles, aldehydes and ketones, Schiff's bases, vinylphosphinic ester and acetates of vinyl alcohols [1]. As a development of these investigations it seemed interesting to determine the possibility of adding to unsaturated compounds the acids of phosphorous themselves, namely, phosphorous, thiophosphorous, alkyl- or arylphosphinous and hypophosphorous acids. As is known, some of these acids are capable of adding at the carbonyl group of aldehydes and ketones [2]. In the present investigation we carried out experiments on the addition of phosphorous and hypophosphorous acids to maleic esters. Achieving these reactions was also of specific interest since it would be a simple method of obtaining acid esters of phosphonosuccinic acid and its salts. These compounds may be considered as phosphorous analogs of the widely used surface-active substance dismulgan, which is the sodium salt of the di-(α -ethylhexyl) ester of sulfonylsuccinic acid. The reaction involved heating a mixture of equimolecular amounts of the maleic ester and phosphorous or hypophosphorous acid for many hours at 90-100°. The addition of hypophosphorous acid proceeded more smoothly than the addition of phosphorous acid: The yields of addition products after 30-32 hours' heating were 60-65 % of (I) and 15-20% of (II), respectively.



As regards the mechanism of these reactions, during the reaction there is apparently gradual isomerization of acids with pentavalent phosphorous to acids with trivalent phosphorous, which then add at the double bond.



Attempts to use alcoholates of alkali metals or tertiary amines as catalysts in these reactions have not as yet led to any essential increase in the yields of addition products or a reduction in the reaction time.

The characteristics of the products obtained by addition of phosphorous and hypophosphorous acids to diethyl, diisooamyl and dioctyl maleates are given in Table 1. They were white or slightly yellow crystalline products, which dissolved readily in water and alcohol and sparingly in ether. Neutralization of the acid esters with NaOH solution gave the disodium salts, which were also readily soluble in water.

TABLE 1

Esters of Phosphonosuccinic Acid

Formula	Boiling point	Yield (in%)	Phosphorus content (in %)	
			found	calc.
$ \begin{array}{c} \text{O} \quad \text{CH}_3-\text{COOC}_2\text{H}_5 \\ \parallel \\ (\text{HO})_2\text{P}-\text{CH}-\text{COOC}_2\text{H}_5 \\ \parallel \\ \text{O} \quad \text{CH}_3-\text{COOC}_6\text{H}_{11}-\text{iso} \end{array} $	265—268°	16.0	11.80	12.20
$ \begin{array}{c} \text{O} \quad \text{CH}_3-\text{COOC}_6\text{H}_{11}-\text{iso} \\ \parallel \\ (\text{HO})_2\text{P}-\text{CH}-\text{COOC}_6\text{H}_{11}-\text{iso} \\ \parallel \\ \text{O} \quad \text{CH}_3-\text{COOC}_6\text{H}_{17} \end{array} $	269—271	17.5	8.79	9.17
$ \begin{array}{c} \text{O} \quad \text{CH}_3-\text{COOC}_6\text{H}_{17} \\ \parallel \\ (\text{HO})_2\text{P}-\text{CH}-\text{COOC}_6\text{H}_{17} \\ \parallel \\ \text{O} \quad \text{CH}_3-\text{COOC}_2\text{H}_5 \end{array} $	270—272	7.0	6.91	7.34
$ \begin{array}{c} \text{O} \quad \text{CH}_3-\text{COOC}_2\text{H}_5 \\ \parallel \\ \text{HO}-\text{PH}-\text{CH}-\text{COOC}_2\text{H}_5 \\ \parallel \\ \text{O} \quad \text{CH}_3-\text{COOC}_6\text{H}_{11}-\text{iso} \end{array} $	250—251	65.0	12.66	13.15
$ \begin{array}{c} \text{O} \quad \text{CH}_3-\text{COOC}_6\text{H}_{11}-\text{iso} \\ \parallel \\ \text{HO}-\text{PH}-\text{CH}-\text{COOC}_6\text{H}_{11}-\text{iso} \end{array} $	252—254	63.0	9.84	9.61

We were also able to add phosphorous acid to maleic acid itself. As in the previous cases, the reaction proceeds with prolonged heating of the reagents in the absence of catalysts. In addition, phosphorous acid was added to n-amyl cinnamate and cinnamic acid itself. Reaction occurred in both cases, but the addition products were obtained as very thick, viscous liquids, which did not crystallize on standing. These products could not be obtained in an analytically pure form despite careful purification.

In previous work we showed that the simplest dialkylphosphorous acids [3] and also ethylphosphonoacetate [4] add to methyl and ethyl maleates in the presence of alcoholates of alkali metals. In connection with recent syntheses of new types of surface-active substances and plasticizers, which are esters of phosphinic and phosphoric acids, it seemed interesting to us to use the method we developed to obtain esters of phosphonosuccinic and α -phosphono- α, β, γ -propanetricarboxylic acids, containing heavier radicals. The addition of dialkylphosphorous acids to maleic esters proceeds according to the equation:



The characteristics of the products obtained are given in Table 2.

The esters of dialkylphosphonosuccinic acid obtained were viscous, colorless liquids, which were difficultly soluble in water and readily soluble in organic solvents.

The addition of phosphonoacetic esters to maleic esters is expressed by the equation:

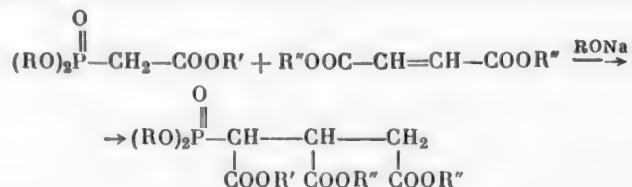
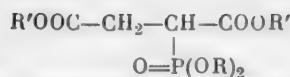


TABLE 2

Esters of Dialkylphosphonosuccinic Acid

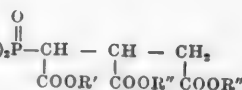


R	R'	Boiling point pressure (in mm)	n_D^{20}	d_4^{20}	$M R_D$		Phosphorus content (%)		Yield (in %)
					found	calc.	found	calc.	
C ₂ H ₅	C ₅ H ₁₁ -iso	167—168 (1)	1.4402	1.0660	99.7	99.44	7.71	7.81	69.3
C ₅ H ₁₁ -iso	C ₂ H ₅	198 (6)	1.4420	1.054	99.17	99.44	7.69	7.81	52.0
C ₅ H ₁₁ -iso	C ₅ H ₁₁ -iso	214—216 (4)	1.445	1.0061	126.4	127.0	6.67	6.5	56.2
C ₈ H ₁₇	C ₈ H ₁₇	209 (2)	1.4455	1.0090	126.2	127.0	6.81	6.55	44.0

The constants of the products obtained are given in Table 3.

TABLE 3

Esters of Dialkylphosphonopropanetricarboxylic Acid



R	R'	R''	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	$M R_D$		Phosphorus content (in %)		Yield (in %)
						found	calc.	found	calc.	
C ₂ H ₅	C ₂ H ₅	C ₄ H ₉ -iso	193° (2.5)	1.4440	1.0840	110.9	110.4	6.71, 6.92	6.85	61
C ₂ H ₅	C ₂ H ₅	C ₄ H ₉	195—196 (2.5)	1.4450	1.0821	110.9	110.4	6.63	6.85	64
C ₂ H ₅	C ₂ H ₅	C ₅ H ₁₁ -iso	212—213 (3.5)	1.4490	1.0790	119.3	119.6	6.7, 6.71	6.45	68
C ₂ H ₅	C ₄ H ₉ -iso	C ₄ H ₉	199—200 (3)	1.4440	1.0710	119.1	119.6	6.31, 6.66	6.45	55
C ₂ H ₅	C ₄ H ₉ -iso	C ₄ H ₉ -iso	204—205 (4)	1.4470	1.0743	119.4	119.6	6.71, 6.74	6.45	61
C ₂ H ₅	C ₄ H ₉ -iso	C ₅ H ₁₁ -iso	220 (8)	1.4479	1.0580	128.5	128.8	6.31, 6.41	6.10	50
C ₂ H ₅	C ₄ H ₉	C ₄ H ₉	222 (5.5)	1.4476	1.0732	119.5	119.6	6.72, 6.61	6.45	65
C ₂ H ₅	C ₄ H ₉	C ₄ H ₉ -iso	220—222 (5)	1.4432	1.0691	119.1	119.6	6.46	6.45	44
C ₂ H ₅	C ₄ H ₉	C ₅ H ₁₁ -iso	232 (10)	1.4441	1.0510	128.4	128.8	6.27	6.10	33

The addition products were colorless or pale straw-colored, viscous liquids with a weak pleasant smell, which were almost insoluble in water, but readily soluble in organic solvents. The addition of dialkylphosphorous acids to maleic esters proceeded very readily in the presence of alcoholates of alkali metals and was accompanied by a considerable exothermic effect. On the contrary, esters of phosphonoacetic acid added with difficulty; it was necessary to heat the reaction mixtures on an oil bath for several hours in the presence of considerable amounts of sodium alcoholate. Evidently, steric factors have an essential effect on the reaction rate.

EXPERIMENTAL

1. Addition of phosphorous and hypophosphorous acids to maleic esters. Equimolecular amounts of phosphorous or hypophosphorous acid and the maleic ester (0.05–0.1 mole of reagents was usually taken) were heated on a boiling

water bath for 30-40 hours. The precipitate was collected and dissolved in alcohol and the solution heated with activated charcoal for 2 hours to free the product from tarry substances. After removal of the alcohol, the residue was treated with ether and recrystallized several times from alcohol.

2. Addition of phosphorous acid to maleic acid. 6 g of phosphorous acid and 8.5 g of maleic acid in 50 ml of anhydrous alcohol were heated for 48 hours with vigorous stirring. After removal of the alcohol, the residue deposited a small amount of maleic acid on prolonged standing in a desiccator. The addition product, as a viscous liquid, was dissolved in anhydrous alcohol and the solution heated for several hours with freshly baked aluminum oxide powder and, after removal of the aluminum oxide, with activated charcoal. Removal of the alcohol and prolonged drying in a desiccator yielded 7.4 g of phosphonosuccinic acid as a very viscous, colorless liquid.

Found %: P 16.14. $C_4H_7O_7P$. Calculated %: P 15.65.

3. Addition of phosphorous acid to amyl cinnamate and to cinnamic acid. a) 3 g of phosphorous acid and 7.9 g of amyl cinnamate were heated with 40 ml of anhydrous alcohol for 48 hours with vigorous stirring. After removal of the alcohol, the viscous liquid was purified as described in the previous experiment. About 2 g of n-amyl β -phenyl- β -phosphonopropionate was obtained as a very thick viscous liquid.

Found %: P 11.12. $C_{14}H_{21}O_5P$. Calculated %: P 10.33.

b) Phosphorous acid was reacted with cinnamic acid under analogous conditions. The reaction product was obtained as a very thick, viscous liquid, which did not crystallize on prolonged standing.

Found %: P 12.55. $C_9H_{11}O_5P$. Calculated %: P 13.48.

4. Addition of dialkylphosphorous acids to maleic esters. To a mixture of dialkylphosphorous acid and maleic ester in equimolecular amounts was added an almost saturated alcohol solution of sodium ethylate with continuous stirring. The reaction proceeded with considerable heat evolution and after a short induction period which was observed at the beginning of the reaction, the temperature of the reaction mixture rose rapidly and reached 100-110°. The addition of the alcoholate was then continued slowly until the addition produced no further increase in the temperature of the reaction mixture. After neutralization of the alcoholate with glacial acetic acid, the reaction mixtures were vacuum distilled.

5. Addition of phosphonoacetic esters to maleic esters. A reaction mixture consisting of 0.04-0.05 mole of phosphonoacetic ester, 0.04-0.05 mole of maleic ester and 1-2 ml of a saturated alcohol solution of sodium ethylate was heated on an oil bath at 100-110° for 5-6 hours. The sodium alcoholate was neutralized with glacial acetic acid and then the reaction mixture was vacuum distilled.

SUMMARY

1. It was shown that phosphorous and hypophosphorous acids add to maleic esters during prolonged heating in the absence of catalysts.

2. The addition of dialkylphosphorous acids and phosphonoacetic esters to maleic esters yielded a series of new esters of phosphonosuccinic and phosphonopropanetricarboxylic acids with butyl, isobutyl and isoamyl radicals in the ester group.

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NEW METHOD OF SYNTHESIZING ESTERS OF PHOSPHINIC AND THIOPHOSPHINIC ACIDS

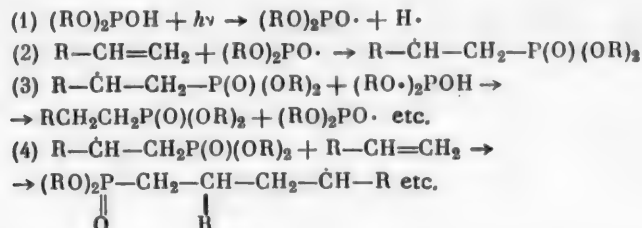
XXXII. ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED HYDROCARBONS

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Kazan Branch of the Motion Picture Scientific Research Institute

We previously showed that dialkylphosphorous acids add to various unsaturated compounds of an electrophilic nature [1]. These reactions proceed by an ionic mechanism in the presence of alcoholates of alkali metals. The addition of dialkylthiophosphorous acids proceeds analogously [2-4].

In the present work we set out to study the addition of dialkylphosphorous acids to unsaturated hydrocarbons and establish the order of addition. There is information on the possibility of this addition in patents [5, 6], which appeared after the publication of our first investigations of the addition of partial esters of phosphorous acids to electrophilic unsaturated compounds. As dialkylphosphorous acids we used dimethyl-, diethyl-, di-n-propyl- and di-n-butylphosphorous acids and the hydrocarbons were a series beginning with hexene and ending with undecene. The reactions did not proceed with heating in the absence of catalysts or in the presence of acid or alkaline catalysts. Satisfactory results were obtained by carrying out the reactions in the presence of benzoyl peroxide or by irradiating the reaction mixtures with ultraviolet light. In these cases, the reactions proceeded by a radical chain mechanism. In the case of photochemical initiation, the following scheme is most probable.



Reactions (1), (2) and (3) produce initiation, chain growth and the formation of an addition product and (4) causes the formation of a polymeric residue due to a further telomerization reaction. The reactions were carried out in the presence of 1.5-2 moles excess of dialkylphosphorous acid for 20-25 hours at 80-90° with continuous irradiation by a mercury-quartz lamp or heating with a small amount of benzoyl peroxide. The two cases gave the same alkylphosphinic esters in 45-60% yield. The length of the radical of the dialkylphosphorous acid had little effect on the yield of the addition product. In all cases, a thick polymeric product was formed, which could not be distilled in normal vacuum.

The alkylphosphinic esters were colorless, mobile liquids, which were almost insoluble in water and readily soluble in organic solvents. Hydrolysis of diethyl cyclohexylphosphinate in the presence of hydrochloric acid yielded crystalline cyclohexylphosphinic acid.

Analogous hydrolysis of esters of alkylphosphinic acids with aliphatic radicals yielded the acids as thick, sirupy liquids. Hydrolysis of the esters with an alcohol solution of sodium hydroxide yielded the disodium salts of

the alkylphosphinic acids as colorless, crystalline substances, which were readily soluble in water to give solutions similar to soap with surface-active properties. The characteristics of the alkylphosphinic esters obtained are given in Table 1.

TABLE 1

Esters of Alkylphosphinic Acids $R'-P(OR)_2$

Nature of		Yield (in %)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	M_{R_D}		Phosphorus content (in %)	
R'	R					found	calc.	found	calc.
C_6H_{13}	C_2H_5	20	125—126 (8.5)	1.4545	1.0421	57.22	57.038	13.99	14.09
C_7H_{15}	CH_3	55	144 (15.5)	1.4330	0.9954	54.33	54.62	14.62	14.89
C_8H_{17}	CH_3	55	156 (14)	1.4350	0.9808	59.07	59.23	13.68	13.98
C_8H_{17}	C_2H_5	60	167 (16)	1.4330	0.9532	68.17	68.47	12.30	12.40
C_8H_{17}	$n-C_3H_7$	69	184 (15)	1.4360	0.9367	77.69	77.70	11.08	11.15
C_8H_{17}	$n-C_4H_9$	65	201 (15)	1.4410	0.9325	86.68	86.93	10.28	10.10
C_9H_{19}	CH_3	52	171 (16)	1.4393	0.9788	63.43	63.84	12.95	13.13
C_9H_{19}	C_2H_5	50	175 (14)	1.4360	0.9497	72.68	73.08	11.90	11.74
$C_{10}H_{21}$	CH_3	26	182 (16)	1.4388	0.9662	68.06	68.45	12.18	12.40
$C_{10}H_{21}$	C_2H_5	37	184 (12)	1.4397	0.9452	77.43	77.70	11.28	11.15
$C_{11}H_{23}$	CH_3	45	192 (20)	1.4438	0.9607	73.03	73.076	11.52	11.74

The structure of the addition product was demonstrated on the example of the reaction of octene-1 and diethylphosphorous acid. Two isomeric octylphosphinic esters could be formed by this reaction. We obtained both of these esters.

Diethyl 1-octylphosphinate was synthesized by the Arbuzov rearrangement by the reaction of triethyl phosphite with 1-bromooctane. Its constants agreed completely with those of the ester obtained by the addition reaction. For comparison, we also synthesized diethyl 2-octylphosphinate (by the reaction of triethyl phosphite with 2-iodooctane). The latter ester, which has a branched radical, boiled at a lower temperature and had

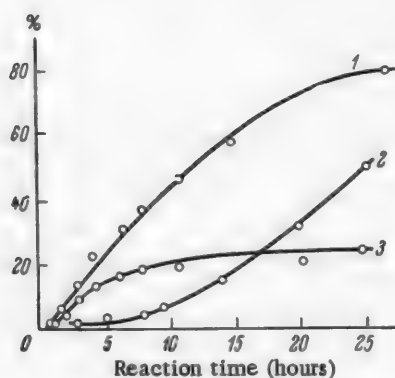


Fig. 1. Kinetics of the reaction of diethylphosphorous acid with cyclohexene under ultraviolet irradiation. 1) Amount of cyclohexene undergoing addition and polymerization; 2) amount of diethylphosphorous acid undergoing reaction; 3) amount of cyclohexene polymerizing.

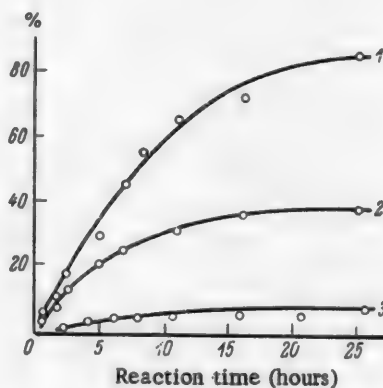


Fig. 2. Kinetics of the reaction of diethylphosphorous acid with octene-1 under ultraviolet irradiation. 1) Amount of octene-1 undergoing addition and polymerization; 2) amount of diethylphosphorous acid undergoing reaction; 3) amount of octene-1 polymerizing.

somewhat different constants from those of the two products described above. The data are presented in Table 2. On the basis of the results obtained, we arrived at the conclusion that the addition of dialkylphosphorous acids to olefins, initiated by light and benzoyl peroxide, proceeds contrary to Markovnikov's rule.

The kinetics of the addition of cyclohexene and octene-1 to diethylphosphorous acid were studied. The rate of the reaction was determined from the change in concentration of diethylphosphorous acid in the reaction mixture, which was determined by titration of a sample with alkali solution, and from the change in concentration of the unsaturated compound, determined by bromination. The yield of phosphinic esters was calculated from the change in concentration of diethylphosphorous acid in the reaction mixtures. The behavior of cyclohexene and octene-1 under irradiation with ultraviolet light was studied in parallel. The data are presented in Figs. 1 and 2. The figures show that together with the formation of the main addition product, telomerization and polymerization of the

TABLE 2

Diethyl Esters of Octyl- and Isooctylphosphinic Acids

Formula of compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Preparation method
$C_8H_{17}P(O)(OC_2H_5)_2$	167-168° (16)	1.4330	0.9532	Addition of diethylphosphorous acid to octene-1
$C_8H_{17}P(O)(OC_2H_5)_2$	167 (15)	1.4330	0.9541	Reaction of triethyl phosphite with 1-bromooctane
iso- $C_8H_{17}P(O)(OC_2H_5)_2$	148-148.5 (14.5)	1.4310	0.9515	Reaction of triethyl phosphite with 2-iodooctane

olefin occur and lead to the formation of a high-boiling residue. Cyclohexene polymerizes much more rapidly than octene-1 under the reaction conditions. It was not possible to decrease the polymerization of cyclohexene or to increase the yield of addition product at all by changing the reaction conditions (increasing the time and changing the temperature). Benzoyl peroxide was found to have a low activity in this reaction. The polymerization process proceeded more slowly in the case of octene-1 (Fig. 2). However, the yield of addition product was limited by the consumption of octene in the telomerization reaction, occurring together with the main addition of diethylphosphorous acid to octene.

In conclusion, the addition of diethylphosphorous acid to hexene-2 and heptene-2 was accomplished. These reactions proceeded more slowly than the addition of dialkylphosphorous acids to olefins with a double bond in the 1,2-position.

EXPERIMENTAL

Olefins with the double bond in a definite position were synthesized by the reactions of organomagnesium compounds with unsaturated compounds of the allyl halide type [7, 8].

Addition of diethylphosphorous acid to octene-1. Experiment I. The reaction mixture, consisting of 12 g of octene-1 and 30 g of diethylphosphorous acid, was placed in a quartz flask and irradiated with a mercury-quartz lamp at a distance of 2-3 cm from it. The reaction lasted for 24 hours at 80-90°. Several vacuum distillations yielded 15.6 g of the addition product, diethyl 1-octylphosphinate, with b. p. 167-168° (16 mm), n_D^{20} 1.4330, d_4^{20} 0.9532.

Experiment II. The reaction mixture, consisting of 10 g of octene-1 and 28 g of diethylphosphorous acid, was heated for 25 hours on a glycerol bath at 80-85°. During the reaction, three 0.15 g portions of freshly recrystallized benzoyl peroxide (m. p. 103°) were introduced into the reaction mixture. The mixture was vacuum distilled. We obtained 13 g of addition product with b. p. 167° (15 mm), n_D^{20} 1.4330, d_4^{20} 0.9532.

Hydrolysis of diethyl cyclohexylphosphinate. 6 g of diethyl cyclohexylphosphinate and a three-fold amount of dilute hydrochloric acid (1:1) were heated for 5 hours in a sealed tube at 140-150°. We obtained 5 g of crystalline cyclohexylphosphinic acid (m. p. 159°).

Found %: P 18.79, 18.70. $C_6H_{11}O_3P$. Calculated %: P 18.90.

Hydrolysis of dimethyl undecylphosphinate. 4.3 g of dimethyl undecylphosphinate and excess of an aqueous alcohol solution of sodium hydroxide were heated under reflux for 14 hours at 150-170°. We obtained 4 g of the disodium salt of undecylphosphinic acid as a white, crystalline mass.

Found %: P 10.50, 10.45. $C_{11}H_{23}O_3PNa_2$. Calculated %: P 11.07.

Addition of diethylphosphorous acid to hexene-2. 16.1 g of hexene-2 and 53.8 g of diethylphosphorous acid were irradiated with a mercury-quartz lamp for 26 hours at 90°. Several vacuum distillations yielded 8.4 g (20%) of diethyl isohexylphosphinate.

B. p. 124-125° (10 mm), d_4^{20} 0.9922, n_D^{20} 1.4380, MR_D 58.75; Calc. 59.23.

Found %: P 13.96, 13.80. $C_{10}H_{23}O_3P$. Calculated %: P 13.96.

Addition of diethylphosphorous acid to heptene-2. 10 g of heptene-2 and 25 g of diethylphosphorous acid were irradiated with a mercury-quartz lamp for 25 hours at 90°. Several vacuum distillations yielded 7.2 g of diethyl isoheptylphosphinate.

B. p. 134° (9 mm), d_4^{20} 0.9761, n_D^{20} 1.4370, MR_D 63.37; Calc. 63.85.

Found %: P 12.95, 12.90. $C_{11}H_{25}O_3P$. Calculated %: P 13.13.

Reaction of 2-iodooctane with triethyl phosphite. 15.5 g of 2-iodooctane and 10.7 g of triethyl phosphite were heated in a sealed tube at 150-160° for 30 hours. Vacuum distillation yielded 5 g of diethyl 2-octylphosphinate.

B. p. 148-148.5° (14.5 mm), d_4^{20} 0.9515, n_D^{20} 1.4310, MR_D 67.95; Calc. 68.47.

Found %: P 12.56, 12.35. $C_{12}H_{27}O_3P$. Calculated %: P 12.40.

SUMMARY

1. It was shown that dialkylphosphorous acids add to unsaturated hydrocarbons in the presence of benzoyl peroxide or during their irradiation with ultraviolet light. The addition products, esters of alkylphosphinic acids, were obtained in yields of ~45-60%.

2. The addition of dialkylphosphorous acids to olefins proceeds by a chain radical mechanism, contrary to Markovnikov's rule.

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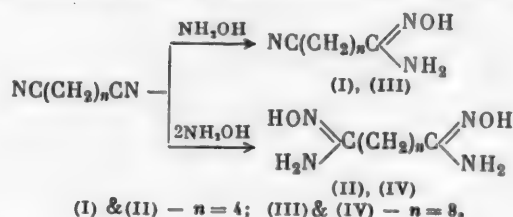
AMIDOOXIMATION OF THE DINITRILES OF ADIPIC AND SEBACIC ACIDS

E. N. Zil'berman and N. A. Rybakova

Diamidooximes of dibasic acids from oxalic to ω,ω' -nonanedicarboxylic acids have been described in the literature [1-3]. The diamidooximes of adipic and sebacic acids are exceptions and there are no data on them.

The purpose of the present work was to prepare the diamidooximes of these two acids from the corresponding dinitriles.

The method usually used for the preparation of amidooximes is based on reaction of the nitrile with hydroxylamine hydrochloride in the presence of base [4]. Amidooximation of adiponitrile by this method gave a very impure product and a small amount of pure product, free from chlorine, could only be isolated with great difficulty. For the amidooximation we therefore used a solution of free hydroxylamine in *n*-butyl alcohol [5], which was obtained by neutralization of hydroxylamine hydrochloride in *n*-butyl alcohol with ammonia. Depending on the amidooximation conditions, we obtained mono- or diamidooximes or the two products together.



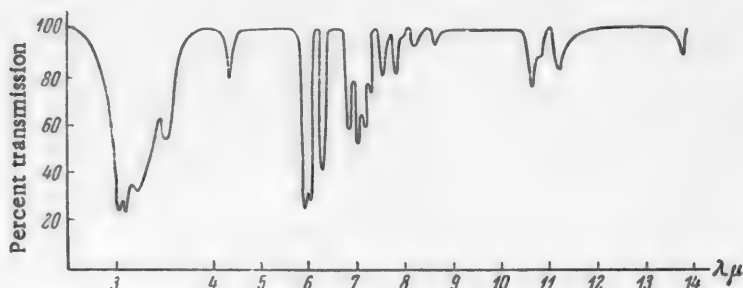
Experiments on the amidooximation of adiponitrile showed (see table) that at 50°, regardless of the ratio of the starting materials, only one of the nitrile groups of the dinitrile reacted and formed the amidooxime of δ -cyanovaleric acid (I). The diamidooxime of adipic acid (II) was obtained only when the temperature was

Amidooximation of the Dinitriles of Adipic and Sebacic Acids

Nitrile	Reaction temperature	Molar ratio of dinitrile and hydroxylamine	Diamidooxime yield (in %)	Monoamidooxime yield (in %)
Adiponitrile	50°	1:1.1	0	76
	50	1:2.2	0	75
	60	1:2.2	26.3	70
	70	1:2.2	47.0	47.8
	80	1:2.2	24.6	45.0
Sebaconitrile	50	1:1.1	15.3	35.2
	50	1:2.2	55.0	40.2
	60	1:2.2	32.8	49.0

raised to 70°. In the case of sebaconitrile, both nitrile groups were amidooximated at 50° and the amidooximes (III) and (IV) were formed. Evidently, the nitrile group of the monoamidooxime (I) has a lower reactivity than a nitrile group of adiponitrile. An analogous phenomenon was observed in the hydrochlorination of adiponitrile where one nitrile group reacted selectively. The reduced reactivity of the second nitrile group is apparently explained by the formation of a weak bond between the nitrogen atom of this group and one of the active hydrogen atoms of the same molecule [6].

The structure of the amidooxime (I) was confirmed by the infrared spectrum (see figure). It contained characteristic frequencies found both in the spectrum of adiponitrile [7] and in the spectrum of the diamidooxime of glutaric acid [5]. The spectrum of the amidooxime (I) had the frequency 4.4 μ , indicating the presence of a $-C \equiv N$ group, and also the frequency 6.04 μ , characteristic of a $-C=N$ -bond.



Infrared spectrum of the amidooxime of δ -cyanovaleic acid (I).

EXPERIMENTAL

Adiponitrile. The technical product was treated with sulfuric acid and then washed with ammonium bisulfate solution [7]. The adiponitrile obtained had a solidification point of 2.4°, d_4^{20} 0.962 and n_D^{25} 1.4369.

Sebaconitrile. 404 g of sebacic acid and 15 g of phosphoric acid were placed in a round-bottomed flask with a wide fractionating column, heated to 200°, and the temperature slowly raised while a stream of ammonia was passed in at 150 liters/hr. At a temperature of 200-295° in the flask, an aqueous fraction was collected and then the ammonia input was increased to 300 liters/hr and a nitrile fraction was collected at a temperature of 295-320° in the flask. After vacuum distillation, the sebaconitrile was washed with dilute sodium carbonate solution and redistilled. We obtained 263 g (80%) of dinitrile.

B. p. 181° (5 mm), d_4^{20} 0.913, n_D^{20} 1.4479.

Literature data [8]: B. p. 198-199° (15 mm), d_4^{20} 0.913, n_D^{20} 1.4474.

Preparation of hydroxylamine. To 20 g of hydroxylamine hydrochloride was added 350 ml of n-butyl alcohol. The mixture was stirred in a flask fitted with a thermometer and reflux condenser, heated to 50°, and gaseous ammonia slowly passed in for 1.5-2 hours. The temperature was maintained at 60-65° during the reaction. After the mixture had cooled to room temperature, the white precipitate of ammonium chloride together with unreacted hydroxylamine hydrochloride was removed by filtration. A solution of free hydroxylamine in n-butyl alcohol was obtained (concentration 22 g/liter, 75% yield).

Amidooxime of δ -cyanovaleic acid (I). To 10.8 g of adiponitrile was added 3.6 g of hydroxylamine in 300 ml of n-butyl alcohol and the mixture kept at 50° for 16-18 hours. The n-butyl alcohol was removed at 70-50 mm. After standing for two days at room temperature, the residue deposited 10.7 g (76%) of amidooxime (I) as white granules with m. p. 89-91° (from a mixture of benzene and alcohol, 1:1).

Found %: C 50.97; H 7.81; N 29.85. $C_6H_{11}ON_2$. Calculated %: C 51.06; H 7.80; N 29.79.

Amidooxime (I), like the other amidooximes described below, gave a characteristic reaction with Fehling's solution [9]. Boiling (I) with 30% sulfuric acid yielded adipic acid with m. p. 152°.

An IKS-12 spectrophotometer (NaCl prism) was used to plot the infrared spectrum of a pressed mixture of amidooxime (I) and KBr [containing 1% of (I) and 99% of KBr].

Diamidooxime of adipic acid (II). To 10.8 g of adiponitrile was added 600 ml of a solution of hydroxylamine in n-butyl alcohol containing 7.2 g of free hydroxylamine and the mixture kept at 70° for 16-18 hours. The diamidooxime (II) precipitated in the form of white crystals even during the reaction; the yield was 8.2 g (47%) and the m. p. 168-170° (decomp., from alcohol).

Found %: C 41.40; H 7.99; N 32.21. $C_8H_{14}O_2N_4$. Calculated %: C 41.38; H 8.04; N 32.18.

After evaporation of the butanol, the mother liquor yielded 6.7 g (47.6%) of amidooxime (I).

Amidooxime of ω -cyanopelargonic acid (III) and diamidooxime of sebacic acid (IV); these compounds were obtained as described above. The diamidooxime (IV) was a white crystalline substance with m. p. 152° (decomp., from alcohol).

Found %: C 52.10; H 9.63; N 24.42. $C_{10}H_{18}O_4N_2$. Calculated %: C 52.17; H 9.57; N 24.30.

The n-butyl alcohol was distilled from the filtrate remaining after separation of (IV). On standing the residue deposited white platelets of monoamidooxime (III) with m. p. 71° (from ether).

Found %: C 60.33; H 9.81; N 21.07. $C_{10}H_{19}ON_2$. Calculated %: C 60.91; H 9.65; N 21.32.

We would like to thank V. S. Étlis for suggesting the method of preparing free hydroxylamine and A. I. Finkel'shtein for plotting the infrared spectrum.

SUMMARY

We prepared the previously undescribed amidooximes of δ -cyanovaleric and ω -cyanopelargonic acids and also the diamidooximes of adipic and sebacic acids.

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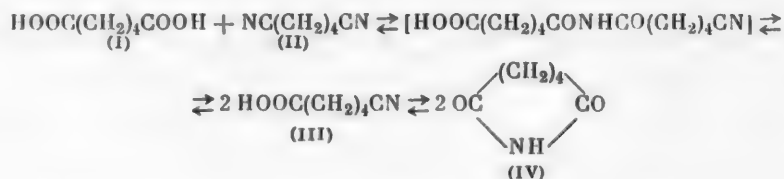
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MECHANISM OF SECONDARY AMIDE FORMATION BY THE REACTION OF NITRILES WITH CARBOXYLIC ACIDS

E. N. Zil'berman

The reaction between organic acids and nitriles was first studied by Gautier [1]. The reaction product he obtained was a secondary amide (diacetylamine). In some cases it is advantageous to add a few drops of acetic anhydride to the reaction mixture to increase the yield of secondary amide [2]. When the aromatic acid is heated with an aliphatic nitrile, instead of a secondary amide, an aliphatic acid and an aromatic nitrile are formed [2]. The reaction of succinic acid and its dinitrile yielded succinimide [3]. From the reaction products of adipic acid (I) and adiponitrile (II), we [4] isolated largely δ -cyanovaleric acid (III) and also a small amount of adipimide (IV).

There are few data in the literature on the mechanism of the reaction between acids and nitriles. In the work mentioned [4], it was proposed that the primary reaction product is the secondary amide, which decomposes to the acid (III) and this is then partially converted into adipimide (IV).



In the present work, the scheme proposed was confirmed and the mechanism of the reaction between carboxyl and nitrile groups was investigated in more detail. For this purpose adipic acid was reacted with adiponitrile at various temperatures, for various times, and in the presence of additives which accelerated or retarded the interconversions of the starting and intermediate compounds. The imide (IV) was isolated from the reaction products and the adiponitrile and δ -cyanovaleric acid (III) contents were determined.

By experiments at different temperatures (Table 1) it was established that the reaction studied proceeded at a moderate rate and without tar formation at 200° and therefore subsequent experiments were carried out at this temperature. Considerable tar formation was observed at 240°. A study of the composition of the reaction products in relation to the reaction duration (see figure) confirmed that δ -cyanovaleric acid (III) was formed initially and adipimide (IV) was formed from it.

However, if a secondary amide were formed by reaction of the nitrile and acid groups of δ -cyanovaleric acid, the reaction between adipic acid and adiponitrile should also have given as the primary product a compound with a secondary amide group, as shown in the scheme presented above. Our attempts to isolate such a compound showed that in contrast to the seven-membered ring of adipimide, it was unstable and under the reaction conditions studied it immediately decomposed as it was formed to give the starting components or two molecules of δ -cyanovaleric acid. Therefore, the rate of formation of acid (III) from adipic acid and adiponitrile was limited by the rate of formation of the secondary amide. Hence additives to the reaction mixture were of interest as accelerators or retarders of the formation of secondary amides from acids and nitriles.

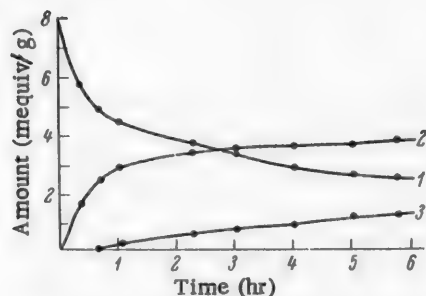
The experiments performed (Table 2) showed that acids catalyze the reaction between adipic acid and adiponitrile. The reaction was also accelerated by tricresyl phosphate, which is capable of forming the acid

TABLE 1

Effect of Temperature on the Reaction of Adipic Acid with Adiponitrile (duration 3 hours)

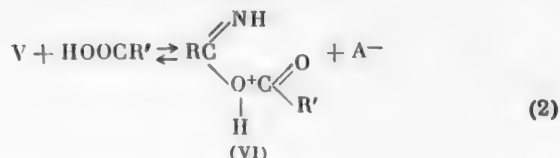
Temperature	Found in mequiv/g of starting mixture		
	adiponitrile	δ -cyanovaleric acid	adipimide
180°	7.8	—	—
200	3.4	3.5	0.75
220	2.7	4.0	0.85
240	2.3	4.8	0.2

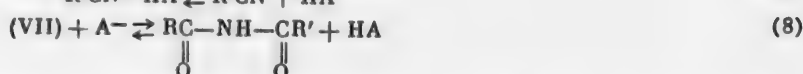
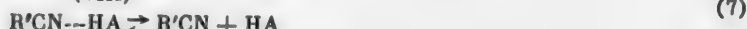
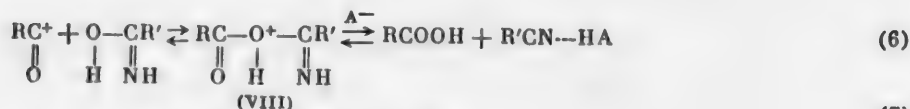
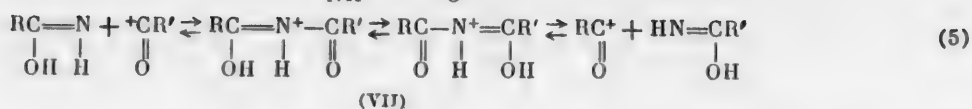
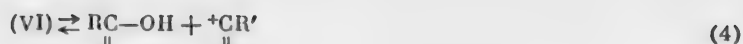
under the experimental conditions (Experiment 12). Experiments in which equivalent amounts of acid were used as additives (Experiments 2 and 4-6) showed that the catalytic effect in general increased with an increase in the dissociation constant of the catalyzing acid. Acids which were weaker than adipic acid (Experiments 9-11) did not accelerate the reaction between adipic acid and adiponitrile. Boric acid (Experiment 8) is not an exception to the general rule as it changes into the strong tetraboric acid at 140° [5]. Nucleophilic dioxane and pyridine appreciably inhibited the reaction between the acid and nitrile (Experiments 13 and 14). From these data we can conclude that the reaction begins with interaction of the unshared electron pair of the nitrogen atom of the nitrile with the acid (Reaction 1). Due to a decrease in electron density, the positive charge on the carbon atom of the nitrile group is increased in the complex formed (V). This causes reaction of (V) with the carboxylic acid and as a result cation (VI) is formed (Reaction 2).



Composition of reaction products relative to the duration of the reaction of adipic acid and adiponitrile at 200°. 1) Adiponitrile; 2) δ -cyanovaleric acid; 3) adipimide.

the carboxylic acid to form the protonated molecule (VI). In the absence of strong acid catalysts, the role of HA in Reaction (1) is played by the carboxylic acid itself, which forms a secondary amide with the nitrile. An isoimide is formed from the cation (VI) (Scheme 3) and this can decompose to the original nitrile and acid. However, (VI) also undergoes other conversions, evidently beginning with rupture of the acyl-oxygen bond to form an acylium ion (4) and then the protonated diacylamine (VII). Depending on the nature of the radicals R and R' and the reaction conditions, (VII) may decompose at the acyl-nitrogen bond (Reaction 5) and form (by Reaction 6) the protonated isoamide (VIII), isomeric with the cation (VI), which readily decomposes to acid and nitrile (Reaction 6 and 7). (VII) may also donate a proton to the anion and form free diacylamine (Reaction 8).





The scheme presented is in accordance with the reactions of secondary amides. It was suggested [6] and demonstrated that, depending on the conditions, N-acyl compounds may change into O-acyl compounds [7] and vice versa [8, 9]. In connection with these properties of secondary amides, an isoimide [O-acyl (B)] and not an imide [N-acyl (A)] structure was ascribed to them for a long time [10].

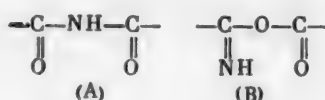


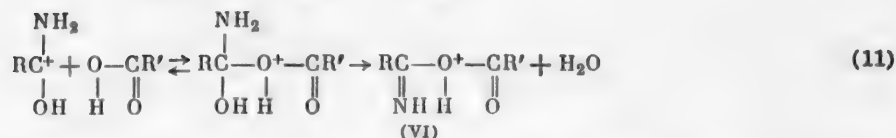
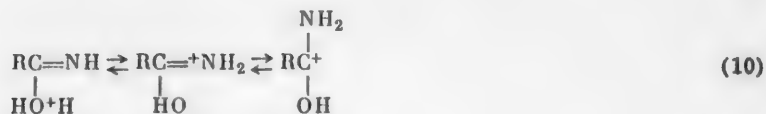
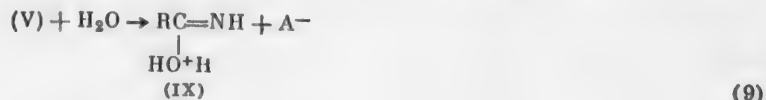
TABLE 2

Products of the Reaction Between Adipic Acid and Adiponitrile in the Presence of Additives (duration 3 hours, temperature 200°)

Expt. No.	Additive		Unreacted adiponitrile (mequiv/g)*	Reaction products (mequiv/g)*		Degree of conversion of adiponitrile (in %)
	name	amount (in wt. %)		δ -cyanovaleric acid	adipimide	
1	—	—	3.4	3.5	0.75	56
2	Phosphoric acid	2.5	2.0	4.8	0.85	74
3	The same	10	0.7	6.1	0.6	91
4	Sulfuric acid	4	1.8	5.0	1.0	77
5	Chloroacetic acid	6	2.3	4.5	0.7	69
6	Benzoic acid	9	3.0	4.0	0.7	61
7	Succinic acid	8	2.9	4.0	0.9	63
8	Boric acid	3	1.3	5.8	0.5	83
9	Acetic acid	5.5	3.45	3.6	0.6	55
10	Sebacic acid	9	3.3	3.4	0.7	55
11	Stearic acid	8	3.7	3.2	0.9	53
12	Tricresyl phosphate	12	3.0	4.0	0.8	62
13	Dioxane	4	4.3	3.1	0.3	45
14	Pyridine	5	4.6	2.9	0.1	39
15	Water	1	3.1	4.0	0.3	58
16	The same	1.6	2.8	4.8	0.2	64
17	Ammonium chloride	3	1.1	6.1	0.4	86
18	Acetic anhydride	2	3.9	3.3	0.4	49
19	The same	4	4.5	3.1	0.2	42

* Amount in milliequivalents per g of starting mixture (after deduction of additives).

The catalytic properties of water are interesting (Table 2, Experiments 15 and 16). Water apparently adds to complex (V) to form the amide in the form of cation (IX) (Reaction 9). As is known [9, 11], in the presence of acid catalysts primary amides are converted into secondary amides with the evolution of ammonia; however, in our case this reaction cannot play an important part as it leads to the regeneration of water. It is more probable that



cation (IX), which exists in a series of tautomeric forms (Scheme 10), condenses with the carboxylic acid to the protonated isoamide (VI) (Reaction 11). However, we cannot exclude the possibility of water as an oxonium ion playing the part of HA in Reaction (1).

The considerable catalytic effect of ammonium chloride attracts attention (Experiment 17). Under the reaction conditions, ammonium chloride is partly dissociated into ammonia and hydrogen chloride [12]. Ammonia then reacts readily with the carboxylic acid to form the amide and water. Thus, in the given case the reaction studied is accelerated both by a strong acid and by water.

The reaction between adipic acid and adiponitrile is retarded by acetic anhydride (Table 2, Experiment 18). This inhibitor binds water which is present in the starting materials in small amounts and may be formed during the reaction. However, as the reaction is further retarded by an increase in the amount of acetic anhydride (Experiment 19), this inhibitor, like dioxane and pyridine, evidently impedes Reaction (2) as a result of its nucleophilic properties.

Thus, in the formation of δ -cyanovaleric acid from adipic acid and adiponitrile, the reaction rate is limited by the rate of the slowest stages of the formation of secondary amides, i. e., the formation of complex (V) and its reaction with carboxylic acid (Reactions 1 and 2). In the presence of water the limiting stages may also be the formation of cation (IX) (Reaction 9) and its reaction with the carboxylic acid (Reaction 11). The exchange of places by the nitrile and acid groups when the secondary amides are more stable is limited by decomposition of the isoamide or amide (Reactions 4 and 5).

It should be noted that in the presence of catalysts (strong acids and water) there is not only an increase in the degree of conversion of the adiponitrile, but also a decrease in the specific content of adipimide in the reaction products (Table 2). Acids and water are evidently catalysts which accelerate the decomposition of the imide when it is heated. The effect of these substances on the decomposition of secondary amides is quite normal as the formation of secondary amides from nitriles and acids and their decomposition to nitriles and acids are two parts of the same equilibrium process like esterification and hydrolysis.

EXPERIMENTAL *

Adiponitrile was purified by treatment with sulfuric acid and ammonium bisulfite [13] and then it had a solidification point of 2.4° and was practically opaque to ultraviolet light at 220-240 m μ . The adipic acid was recrystallized from water and dried to constant weight. All the substances whose effect on the reaction was studied were also dried carefully to remove moisture from them as completely as possible.

Experimental procedure. A mixture of 1.4-1.8 g of adipic acid, an equivalent amount of adiponitrile, and the catalyst (or inhibitor) was placed in a tube 10-12 mm in diameter. The sealed tube was heated in a

* Together with M. M. Bershtein.

thermostat. The duration of heating and temperature are given in the tables and the figure. The temperature varied over a range of $\pm 3^\circ$. Two or three parallel experiments were carried out. Average data are given in the tables and figure.

The reaction product was dissolved in 50 ml of boiling water, cooled, and the adipimide precipitate collected by filtration. The solution obtained was neutralized to a mixed indicator (a mixture of equal volumes of 0.1% solutions of Bromthymol Blue and Phenol Red in 20% alcohol), 10 g of sodium sulfate added, and the solution extracted with benzene (3 x 50). The nitrogen contents of the benzene and the aqueous residue were determined [14]. The nitrogen in the extract corresponded to the amount of unreacted adiponitrile and that in the water, to the amount of δ -cyanovaleic acid formed. The weight of adipimide and the nitrogen contents of the two solutions were converted to milliequivalents per g of starting mixture (after deduction of additives).

SUMMARY

1. The effect of temperature, heating time, and the presence of additives on the formation of δ -cyanovaleic acid from adipic acid and adiponitrile was studied.
2. It was shown that strong acids and water catalyze the formation of secondary amides when carboxylic acids are heated with nitriles. In contrast to water, such nucleophilic compounds as acetic anhydride, dioxane, and pyridine are inhibitors of the reaction. A mechanism is proposed for the reaction between acids and nitriles.

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ION EXCHANGE OF COMPLEX SALTS OF PYRIDINE AND QUINOLINE BASES

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The study of ion or isotope exchange of complex salts of pyridine and quinoline bases is of practical and scientific interest. Determining the possibility of applying the isotope dilution method to the analysis of these compounds is of particular practical interest. Chemical and many physical methods cannot be used to solve this problem as almost all the base components, especially isomers, have similar chemical and physical properties. Meanwhile, the successful development of analytical methods involving the use of radioactive isotopes opens up wide prospects of their application to the analysis of coal-tar chemical bases. However, our chemical industry does not produce radioactive preparations in the form of individual base components, with the exception of pyridine [1]. The preparation of such compounds presents very great difficulties. However, radioactive preparations in the form of complex salts of bases can be obtained without any difficulty. The use of such compounds, if only in the isotope dilution method, would make it possible to solve the problem of analyzing the bases mentioned above. As is known, the isotope dilution method is intended for determining the amount of some substance in a complex mixture when its quantitative isolation either involves very great difficulties or is completely impossible.

From the principle of this method it follows that it can only be applied successfully when ion or isotope exchange is absent or is very slight. From the properties of different complex salts one would expect isotope exchange and also in the case of complex salts of bases [2, 3], though to a considerably lesser extent than for inorganic salts. If this exchange were absent or very slight, the isotope dilution method could solve the problem of determining the individual base components in mixtures of them.

The study of ion or isotope exchange of complex salts of bases extends our knowledge both of the structure of these substances and of their behavior. This is all the more important as many technological problems on the isolation of individual components from crude bases remain unsolved at the present.

EXPERIMENTAL

Characteristics of compounds. Quinoline and isoquinoline were chosen as examples of heavy bases for investigation and γ -picoline, as a light one. The characteristics of these substances are given in Table 1.

Quinoline and isoquinoline sulfates were prepared from normal sulfuric acid and from sulfuric acid containing radioactive sulfur, S^{35} . After many recrystallizations from alcohol, these sulfates had the following melting points: Quinoline sulfate 164-164.5°, radioactive quinoline sulfate 164-164.4°, isoquinoline sulfate 207-209°, and radioactive isoquinoline sulfate 207-209°. From γ -picoline we prepared its calcium chloride salt, which is used for isolating γ -picoline from light bases. This salt was prepared both from stable calcium chloride and from calcium chloride containing the radioactive isotope of calcium, Ca^{45} . A comparison of the physical constants of the bases used with literature data [4, 5] indicates that these substances were sufficiently pure.

Investigation procedure. There are two methods of measuring absolute and relative β -particle activities. Either a correction is introduced for self-absorption by the preparation or a sufficiently large amount of material is used for complete absorption of the β -particles in the layer of the preparation examined. Neither of these methods could be used for our activity measurements as we expected that after exchange, the substances interesting us would be in very small and different amounts. In this case their activities could not be compared.

TABLE 1
Physical Properties of Bases

Base	Boiling point	Melting point
Quinoline	237.7-238.7°	—
Isoquinoline	243.4-243.9	24.0-24.5°
γ -Picoline	143.5-144.0	3.0

TABLE 2
Amount of Isoquinoline Sulfate in Artificial Mixture

Weight of tracer and substance isolated (in g)	Activity (counts/min)		S ₁	S ₂	X
	tracer	substance isolated			
0.002	169	9	84500	4500	3.5
0.008	500	27	62500	3375	3.4
0.012	686	37	57166	3083	3.5
0.024	1025	60	42772	2500	3.2
Average					3.4

As a result, we developed a special method of comparing activities, which, in essence, was as follows. A complete curve of the change in radiation intensity in relation to layer thickness was plotted for the substance investigated. Then the substance isolated after the exchange reaction was divided into three or four portions. In the measurement of the activity of this substance, each portion was mixed with the next one to give a sufficient number of points for constructing a curve showing the change in radiation intensity relative to the amount of substance extracted after exchange. Thus, in addition to the self-absorption curve of the original radioactive substance (Curve 1), we constructed an incomplete self-absorption curve of the substance isolated (Curve 2) (Fig. 1). Since both of these curves were constructed in the same coordinates, perpendiculars to the axis, intersecting these curves in any points, must show the activities of both the starting preparation (A) and the one analyzed (B) at the same sample weight, specific volume or surface. This method made it possible not only to compare the activity values, but also to check the reliability of the values obtained, which theoretically should lie on their own self-absorption curve. If the points obtained experimentally lay accurately on the curve, this indicated the reliability and accuracy of the experimental data.

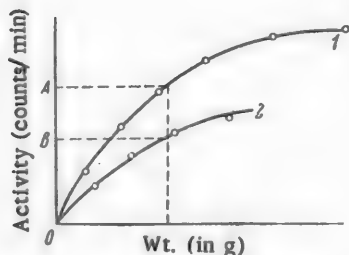


Fig. 1. Self-absorption curves of the radioactive starting material (1) and that isolated from the mixture (2).

and ground in the presence of a small amount of benzene. The finely disperse suspension obtained was poured into a special dismountable beaker, the bottom of which consisted of an aluminum disc. The suspension was also dried to constant weight and then the aluminum disc with the substance investigated was placed in a lead castle for activity measurement.

Results of investigation. Samples for activity measurement were prepared in the following way. The substance obtained after many recrystallizations was dried to constant weight under an electric lamp and then its melting point determined. When the required melting point had been reached, the dry substance was transferred to a porcelain mortar

Figure 2 (Curve 1) gives data showing the change in radiation intensity of the radioactive quinoline sulfate studied in relation to the sample weight or, more accurately, the sample thickness as the sample area was constant. Radioactive quinoline sulfate (0.1 g) was mixed with 2 g of stable isoquinoline sulfate and 0.9 g of stable quinoline sulfate. This mixture was then repeatedly recrystallized from alcohol (time 8-10 minutes) to yield isoquinoline sulfate [4] with m. p. 207-209°. The intensity of its radiation relative to sample weight is shown in Fig. 2 (Curve 2).

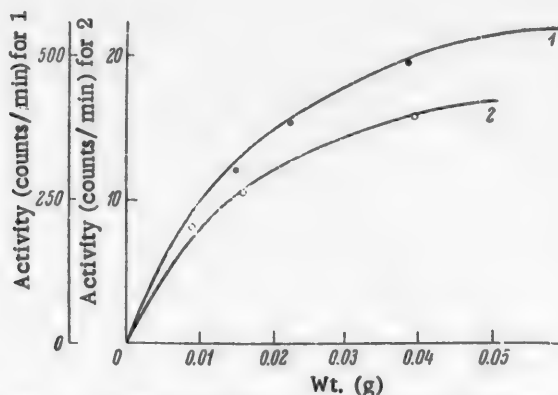


Fig. 2. Radiation intensity of radioactive quinoline sulfate (1) and isoquinoline sulfate (2) isolated from mixture.

The data obtained show that the isoquinoline sulfate isolated from the mixture had a considerable radioactivity. This could be explained by the fact that the radioactive anions of the quinoline sulfate exchanged with the inactive anions of the isoquinoline sulfate. Thus, for example, for 0.02 g of preparation the radiation intensity of the original radioactive quinoline sulfate was 365 counts per minute or the specific activity was $365/0.02 = 18250$ counts/min. g. For a 0.1 g sample of active quinoline sulfate the specific radioactivity of the mixture should be $(18250 \cdot 0.1)/3 = 608$ counts/min. g. After separation of this mixture, the specific radioactivity of a 0.02 g sample of the isoquinoline sulfate isolated was also found to equal $12.0/0.02 = 600$ counts/min. g. In other words, the radioactivity of the isoquinoline sulfate isolated was found to be the same as that of the original mixture.

Similar data are obtained if calculations are made for other sample weights within the range of the self-absorption curves obtained experimentally. For example, for a 0.04 g sample the specific activity of the radioactive quinoline sulfate $510/0.04 = 12750$ counts/min.g; the specific activity of 3 g of mixture $(12750 \cdot 0.1)/3 = 425$ counts/min.g; the specific radioactivity of the isoquinoline sulfate isolated was also found to be $16/0.04 = 400$ counts/min.g.

TABLE 3
Radiation Intensity of Residue Isolated from Filtrate

Sample (In g)	Activity (after subtraction of background) (counts/min)
0.102	{ 35
	{ 36
0.0164	{ 46
	{ 43
	{ 44
0.0235	{ 54
	{ 51
	{ 53

Similar results were obtained when isoquinoline sulfate was used as the radioactive indicator. For the investigation we used an artificial mixture of the following composition: 1.0 g of stable quinoline sulfate, 1.8 g of stable isoquinoline sulfate, and 0.2 g of radioactive isoquinoline sulfate; the total amount of mixture was 3.0 g.

Data on the radiation intensity are shown graphically in Fig. 3. According to these data the following results

for the analysis of the mixture (Table 2) were obtained from the isotope dilution formula:

$$mS_1 = (m + x)S_2, \quad (1)$$

where S_1 is the specific activity of the radioactive tracer, S_2 the specific activity of the substance sought, isolated from the mixture, m the weight of radioactive tracer in the mixture (equal to 0.2 g), and x the weight of the substance sought.

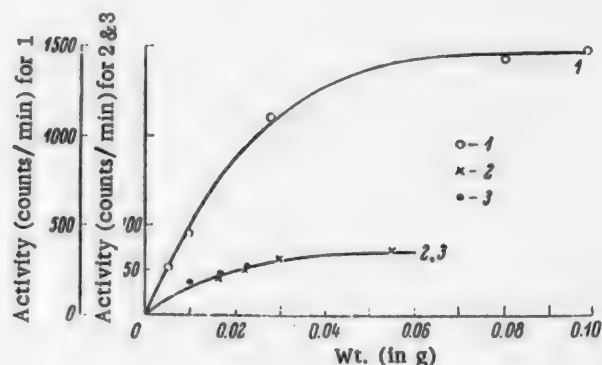


Fig. 3. Radiation intensity of radioactivity isoquinoline sulfate (1), isoquinoline sulfate isolated from mixture (2), and residue isolated by evaporation of filtrate (3).

Thus, analysis by isotope dilution indicated that the mixture contained 3.4 g of isoquinoline sulfate when there was actually 1.8 g present. Since the amount found was determined from the ratio of the specific activities, there had evidently been a decrease in the specific activity of the radioactive tracer by a factor equal to the ratio of 3.4 to 1.8, i. e., almost 2.

TABLE 4

Degree of Exchange of SO_4^{2-} Ions in Solutions of Quinoline and Isoquinoline Sulfates

Weight of tracer and substance isolated (in g)	i_2	i_1	i_3	\bar{x} (%)
0.002	2	169	16.9	47
0.008	27	500	50.0	46
0.012	37	686	68.6	47
0.024	60	1025	102.5	42
Average				45

It is clear that the decrease in specific activity could only occur as a result of the exchange of ions of the radioactive isoquinoline sulfate with ions of the stable isoquinoline and quinoline sulfates.

The data obtained and the calculations were also confirmed by the values of the activity of the residue isolated by drying the filtrate, which contained mainly quinoline sulfate (Table 3).

The data obtained actually lay on one curve (2 and 3, Fig. 3). This indicates that the intensity of the radiation from the isoquinoline sulfate isolated from the mixture was the same as that of the filtrate or, more accurately, the residue isolated from the filtrate.

By using the radioactivity values found (Table 2) it is possible to calculate the degree of exchange from the formula:

$$x = \left(1 - \frac{i_1}{i_2}\right) \cdot 100\% \quad (2)$$

where i_1 is the activity of the tracer (counts/min) and i_2 is the activity of the substance isolated (counts/min).

However, this formula cannot be applied directly in the form presented as the solution contained not only radioactive, but also stable isoquinoline sulfate. Their ratio in the solution was the same as that in the pure isoquinoline sulfate isolated. Consequently, the actual activity of the tracer was $i_3 = (i_1 \cdot 0.2)/(0.2 + 1.8)$, where

TABLE 5

Degree of Exchange of Calcium Ions in Solutions of the Calcium Chloride Salt of γ -Picoline and Calcium Chloride

Weight of tracer and substance isolated (in g)	i_2	i_1	x (%)
0.1	3700	6850	46
0.15	3900	7500	48
0.2	4100	7900	49
0.25	4150	8300	49
Average			48

the amount of radioactive isoquinoline sulfate was 0.2 g and the amount of stable isoquinoline sulfate, 1.8 g.

Table 4 gives the results of calculating the degree of exchange of the SO_4^{2-} ion in solutions of quinoline and isoquinoline sulfates. As the data in Table 3 show, the degree of exchange was about 50%. This calculation agrees completely with the results of analysis by the isotope dilution method, according to which the activity of the tracer decreased by a factor of almost two.

Similar results were obtained on studying the exchange of the calcium chloride salt of γ -picoline with calcium chloride. The exchange was studied in the following way. Crystalline calcium chloride (10 g) was mixed with 1 ml of water and heated to boiling. Then, to the boiling solution was added 0.5 g of the radioactive calcium chloride salt of γ -picoline; after 8-10 minutes the boiling solution was filtered and the precipitate obtained dried. Due to the lack of a method of checking the purity of the complex obtained, in these experiments there was no guarantee that there was no partial precipitation of calcium chloride together with the complex. Some indication of the fact that calcium chloride did not precipitate was provided by the fact that the weight of the precipitate was considerably less than that of the complex salt added. However, this phenomenon could be the result of partial decomposition of the complex since the latter was in contact with calcium chloride solution at its boiling point. Figure 4 gives data on the radiation intensity of the calcium chloride salt of γ -picoline both before and after mixing with calcium chloride solution.

By using Formula (2), but without any corrections in this case, we calculated the degree of exchange of calcium ions (Table 5).

As the data in Table 5 show, the degree of exchange of calcium ions was about 50%, i.e., the same as for the ions in isoquinoline sulfate. Due to the high degree of ion and molecular exchange, the calcium chloride salt of γ -picoline and also the heavy base sulfates could not be used as tracers in the isotope dilution method. Attention is attracted by the fact that the rate and degree of exchange of different ions of salts, attached to a

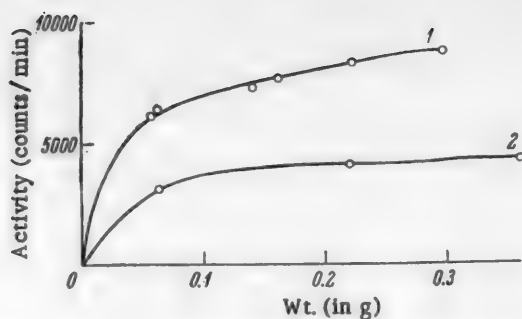


Fig. 4. Radiation intensity of calcium chloride of γ -picoline before (1) and after (2) mixing with calcium chloride solution.

pyridine nucleus, are almost identical. This interesting fact indicates that the cation and anion of the salts investigated are attached to the pyridine nucleus identically. Unfortunately, we were unable to determine the degree of chlorine exchange in the calcium chloride salt of γ -picoline and of hydrogen exchange in the sulfuric acid of quinoline and isoquinoline sulfates and therefore the conclusion drawn is of a preliminary nature. However, if we consider that for this class of compounds, molecules and ions with the same rate and degree of exchange have the same type of bond [6], then the data obtained cast doubt on the accuracy of the formulas of pyridine and quinoline bases [7] in which the differences in the bonds of the cation and anion are emphasized.

SUMMARY

1. A special method of comparing radiation intensities was developed for applying the isotope dilution method to the analysis of very small amounts of materials.
2. It was shown that there is considerable ion and molecular exchange in the calcium chloride salt of γ -picoline and in quinoline and isoquinoline sulfates. This made it impossible to use the isotope dilution method for determining separate homologs of pyridine bases through their complex salts.
3. It was shown that the rate and degree of exchange of the different ions of the salts attached to the pyridine nucleus were almost identical.
4. The data obtained do not confirm the difference in the bonds of anions and cations in the formulas of salts of pyridine bases.

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BENZ-(c,d)-INDOLINE DERIVATIVES

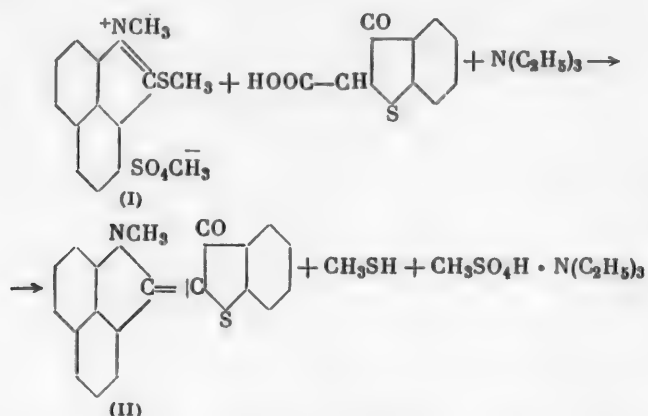
IV. CONDENSATION PRODUCTS OF 1-METHYL-2-METHYLTHIOBENZ-(c,d)-INDOLINIUM METHYLSULFATE WITH 3-HYDROXYTHIONAPHTHENES

N. S. Dokunikhin, G. M. Oksengendler, and Ya. B. Shteinberg

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The method described previously [1] was used to synthesize dyes from derivatives of N-methylbenz-(c,d)-indoline and 3-hydroxythionaphthenes. The compounds synthesized were analogous in structure to the condensation products of thionaphthostyryl and 3-hydroxythionaphthenes [2].

Reaction of 1-methyl-2-methylthiobenz-(c,d)-indolinium methylsulfate (I) with 3-hydroxythionaphthene-2-carboxylic acid yielded a red-violet dye (II).



Condensation of (I) with substituted 3-hydroxythionaphthenes, 6-ethoxy-, 6-chloro-, and 6-chloro-4-methyl-3-hydroxythionaphthene, yielded dyes (III), (IV), and (V), which were similar in shade. Reaction of (I) with benz-3-hydroxythionaphthenes, 4,5-benz- and 1'-chloro-6,7-benz-3-hydroxythionaphthenes formed deeper colored substances (VI) and (VII).

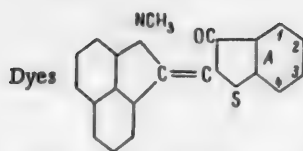
All the substances obtained had a very sharply expressed maximum in the visible region of the spectrum. The benzthionaphthene derivatives (VI) and (VII) showed an additional absorption band of low intensity in the shortwave part of the spectrum (λ 400-470 m μ) (see Table 1). Comparison of dyes (III), (IV), and (V) with the unmethylated analogs described previously [2] showed that the introduction of a methyl group into the benz-(c,d)-indoline nucleus led to a hypsochromic shift in the absorption maximum and eliminated one of the main absorption bands.

The absorption spectra were plotted in m-xylene solution on an SF-2M spectrophotometer.

The compounds synthesized were insoluble in water, but dissolved readily in organic solvents, especially benzene.

* Original Russian pagination. See C. B. Translation.

TABLE 1



Substance No.	Position of substituents in ring A	λ_{\max} (in m μ)	$\epsilon \cdot 10^4$
(II)	—	551	2.67
(III)	3-OC ₂ H ₅	540	2.49
(IV)	3-Cl	550	2.74
(V)	1-CH ₃ , 3-Cl	548	2.61
(VI)	1,2-	428, 563	0.81, 2.98
(VII)	3,4-	432, 566	0.81, 2.64

In an aqueous suspension, dyes (II)-(V) imparted a red-violet tone to acetate and caprone fibers. Dyes (VI) and (VII) gave a violet color to caprone fibers only.

TABLE 2

Dye	Yield of crude substance (in %)	Melting point	Empirical formula	Analysis results (calculated values in brackets)
(II)	52	149.5—151°	C ₂₀ H ₁₃ ONS	C 75.84, 75.90 (76.19); H 4.19, 4.16 (4.12); S 10.02, 10.19 (10.17)
(III)	80	190—191	C ₂₂ H ₁₇ O ₂ NS	N 3.84, 3.89 (3.89); S 8.62, 8.50 (8.92)
(IV)	63	190—190.5	C ₂₀ H ₁₂ ONSCl	C 68.24, 68.31 (68.67); H 3.32, 3.30 (3.43); Cl 9.81, 9.89 (10.13)
(V)	77	218—219	C ₂₁ H ₁₄ ONSCl	N 4.13, 3.98 (3.85)
(VI)	66	215—216	C ₂₄ H ₁₅ ONS	C 79.06, 78.90 (78.93); H 4.22, 4.37 (4.13); N 3.86, 3.88 (3.84); S 8.64, 8.61 (8.78)
(VII)	50	272—273	C ₂₄ H ₁₄ OSCl	C 72.78, 72.46 (72.11); H 3.61, 3.83 (3.50); N 3.45, 3.45 (3.50)

EXPERIMENTAL

Equimolecular amounts of (I) and the appropriate 3-hydroxythionaphthene (0.0025 mole) were boiled for 1 hour in anhydrous alcohol (~10 ml) in the presence of triethylamine (0.0031 mole), cooled, and the product collected by filtration; in the synthesis of (II), (III), and (V), the mixture was first diluted with water. Dyes (II), (III), (IV), (VI), and (VII) were purified by chromatography of a benzene solution on a column packed with Al₂O₃ (the dyes were eluted with benzene with a few drops of alcohol added per 100 ml of benzene) and then

recrystallized from benzene. Dye (V) was purified by four recrystallizations from aqueous alcohol. Data on the dyes obtained are given in Table 2.

SUMMARY

Condensation of 1-methyl-2-methylthiobenz-(c,d)-indolinium methylsulfate with substituted 3-hydroxy-thionaphthenes yielded dyes which colored acetate and caprone fibers.

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*Original Russian pagination. See C. B. translation.

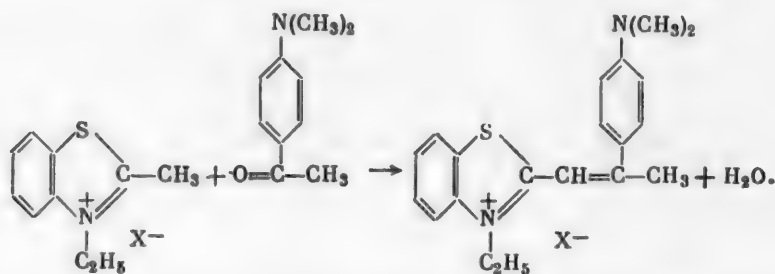
CHEMISTRY OF CYANINE DYES

XIV. CONDENSATION OF AROMATIC AND HETEROCYCLIC KETONES WITH QUATERNARY SALTS OF 2-METHYLBENZTHIAZOLE AND CONVERSION OF THE COMPOUNDS OBTAINED INTO CYANINE DYES

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We previously showed [1] that p-dimethylaminoacetophenone and p-dimethylaminobenzophenone condense with quaternary salts of 2-methylbenzthiazole when heated in acetic anhydride to form β -aryl substituted 2-propenylbenzthiazole, for example:



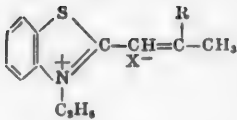

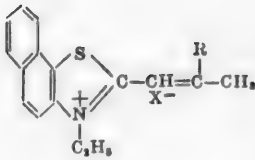

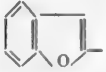
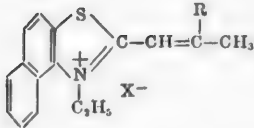


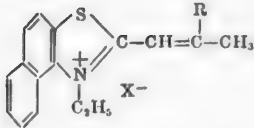
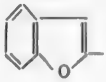
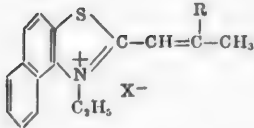

It should be noted that β -phenyl-2-propenylbenzthiazole was synthesized by the action of β -phenylcrotonic anhydride on o-aminothiophenol and conversion of the base into the quaternary salt. Heating the latter with the iodoethylate of 2-methylmercaptobenzthiazole in anhydrous alcohol with the addition of triethylamine formed 9-phenylthiacarbocyanine [2].

In 1951, A. I. Kiprianov, I. K. Ushenko, and G. M. Oksengendler established [3] that acetophenone and β -acetylnaphthalene condense with the methylmethylsulfate of 2-methylbenzthiazole to form iodomethylates of 2- β -phenyl- and 2- β -(β' -naphthyl)-propenylbenzthiazoles. These compounds were condensed with the iodomethylate of 2-methylmercaptobenzthiazole to form several 3,3'-dimethyl-9-arylthiacarbocyanines.

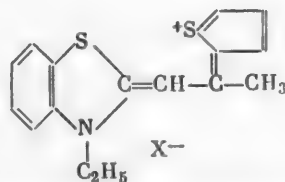
In recent years we have condensed the following aromatic and heterocyclic ketones with quaternary salts of 2-methylbenzthiazole: Acetophenone, p-dimethylaminoacetophenone, p-methoxyacetophenone, o-methoxyacetophenone, p-hydroxyacetophenone, o-hydroxyacetophenone, p-acetylaminoacetophenone, p-nitroacetophenone, methyl mesityl ketone, α -acetylnaphthalene, α -acetylthiophene, α -acetylfuran, α -acetylcoumarone, and methyl 2-benzthiazolyl ketone. It was established that ethyl-p-toluenesulfonates of 2-methylbenzthiazoles condense with ketones much more readily than methylmethylsulfates or ethylethylsulfates of the same bases. The unreacted starting materials could be partially recovered. Fusion of quaternary salts of 2-methylbenzthiazole with aromatic or heterocyclic ketones formed a large amount of tar and therefore the condensation was best carried out in acetic anhydride. As a result of the condensations we obtained the quaternary salts of β -substituted 2-propenylbenzthiazoles listed in Table 1.

TABLE 1

Quaternary Salts of β -Substituted 2-Propenylbenzthiazoles

General formula	R	Absorption maximum (in m μ)
	C ₆ H ₅	355
	C ₆ H ₄ N(CH ₃) ₂ P	529
	C ₆ H ₄ OCH ₃ P	398
	C ₆ H ₄ OCH ₃ O	—
	C ₆ H ₄ OH-P	—
	C ₆ H ₄ OH-O	—
	C ₆ H ₄ NHCOCH ₃ P	396
	C ₆ H ₄ NO ₂ P	—
	C ₁₀ H ₇ -a	—
		413
		412
		428
	C ₆ H ₅	—
	C ₆ H ₄ OCH ₃ P	—
		—
		—
		—
	C ₆ H ₅	—
	C ₆ H ₄ OCH ₃ P	—
		—

The deep color of some quaternary salts of β -substituted 2-propenylbenzthiazoles may be explained by the fact that the positive charge on the quaternary nitrogen atom of the benzthiazole may be transferred along the conjugation chain to the oxygen, nitrogen, or sulfur atom.

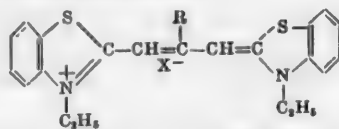


Quaternary salts of β -substituted 2-propenylbenzthiazoles are vinylene homologs of 2-methylbenzthiazole and the hydrogen atoms of the methyl group are very labile. They readily condense with quaternary salts of 2-methylmercaptobenzthiazole and 2-acetanilidovinylbenzthiazole and with 3-ethyl-5-(acetanilidomethylene)-rhodanine and p-dimethylaminobenzaldehyde to form 9-substituted thiacyanines, dicarbothiacyanines, and tetramethynemerocyanines.

Condensation of quaternary salts of β -substituted 2-propenylbenzthiazoles with orthoformic ester formed tricarbocyanines in extremely small amounts.

TABLE 2

9-Substituted Thiocarboyanines



Substance No.	R	Absorption maximum (in m μ)	Displacement of absorption maximum (in m μ) in comparison with(A)
A	H	558	—
I	CH ₃	544	—14
II	C ₂ H ₅	549	—9
III	C ₆ H ₅	561	+3
IV	C ₆ H ₄ N(CH ₃) ₂ -p	562	+4
V	C ₆ H ₄ OCH ₃ -p	562	+4
VI	C ₆ H ₄ OCH ₃ -o	561	+3
VII	C ₆ H ₄ NHCOCH ₃ -p	562	+4
VIII	C ₆ H ₄ NH ₂ -p	560	+2
IX	C ₆ H ₄ OH-p	562	+4
X	C ₆ H ₄ OH-o	562	+4
XI	C ₆ H ₄ O ⁻ -p	562	+4
XII	C ₆ H ₄ O ⁻ -o	562	+4
XIII	C ₁₀ H ₇ - α	563	+5
XIV	C ₆ H ₄ NO ₂ -p	570	+12
XV		575	+17
XVI		580	+22
XVII		585	+27
XVIII		575	+17

Table 2 lists some of the 9-substituted thiocarboyanines we obtained by condensing propenyl derivatives with the iodoethylate of 2-methylmercaptobenzthiazole. The data in Table 2 show that alkyl groups in Position 9 considerably displaced the absorption maximum of thiocarboyanines into the shortwave region of the spectrum, while the absorption maximum of 9-arylthiocarbocyanines differed little from that of unsubstituted thiocarboyanine. This peculiarity of 9-phenylthiocarbocyanine has already been reported by van Dormael [4], who explained it by the fact that the phenyl radical in Position 9 suffers steric hindrance (Fig. 1) and being forced out of the plane of the benzthiazole nuclei, no longer affects the color. It is known that electronic displacements along conjugation chains, characteristic of any dye molecule, occur only in planar molecules [5].

It is interesting that the addition of alkali to an alcohol solution of 9-p-hydroxyphenyl- or 9-o-hydroxy-phenylthiocarbocyanine did not change the absorption maximum at all.

It should be noted that the introduction of a p-nitrophenyl radical into Position 9 of 3,3'-diethylthiocarbocyanine produced a considerable displacement of the absorption maximum into the longwave region of the spectrum.

The data in Table 2 also show that the introduction of heterocyclic radicals into Position 9 of the polymethyne chromophore produces an even greater displacement of the absorption maximum into the longwave region.

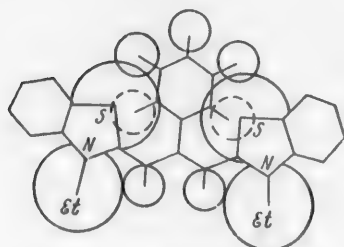


Fig. 1. Steric configuration of 3,3-diethyl-9-phenylthiacarbocyanine.

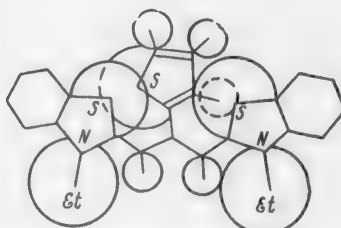


Fig. 2. Steric configuration of 3,3-diethyl-9-(α -thienyl)-thiacarbocyanine.

Figure 2 shows the steric configuration of the 9- α -thienylthiacarbocyanine. It is possible that the reason for the deep color of dye (XIII) is that the α -thienyl radical occupies less space than the phenyl and is therefore not completely forced out of the plane of the thiacarbocyanine molecule and to some extent retains its electronic effect on the color and being a negative radical in the meso position, it deepens the color [6]. This explanation is confirmed by the fact that the α -furyl radical affects the absorption more strongly than the α -thienyl. The effective radius of an oxygen atom is known to be considerably less than that of a sulfur atom (0.66 and 1.04 Å, respectively).

Syntheses of 9-thienyl- and 9-furylthiacarbocyanines are given in patents [7, 8] but they are quite complicated. It is curious that the addition of acid to an alcohol solution of dye (XVI) produced a deepening of color and the absorption maximum was displaced to 583 m μ . The deepening in color was connected with the production of the cationic charge on the benzthiazole nucleus and the consequent increase in negative character of the substituent. It is known [6] that negative substituents in Position 9 of thiacarbocyanine deepen the color. Table 3 lists the benzo- and dibenzothiacarbocyanines we prepared with phenyl and heterocyclic radicals in the meso position. The data in this table show that the absorption maxima of 9-phenyldibenzothiacarbocyanines differ little from those of unsubstituted dyes. In this case also the introduction of heterocyclic radicals into the meso position considerably displaced the absorption maxima into the longwave region.

In 1952 N. N. Sveshnikov and N. S. Stokovskaya showed that the iodoethylates of 2- β -phenyl- and 2- β -methylpropenylbenzthiazoles condense with 3-ethyl-2-formylmethylenebenzthiazoline to form 9-substituted thiadicarbocyanines. [9]. We established that quaternary salts of 2- β -arylpropenylbenzthiazoles readily condense with the iodoethylate of 2-acetanilidovinylbenzthiazole, 3-ethyl-5-(acetanilidomethylene)-rhodanine, and p-dimethylaminobenzaldehyde to form 9-aryl substituted thiadicarbocyanines, β -aryl substituted tetramethynemerocyanines, and vinylene homologs of styryl dyes, for example:

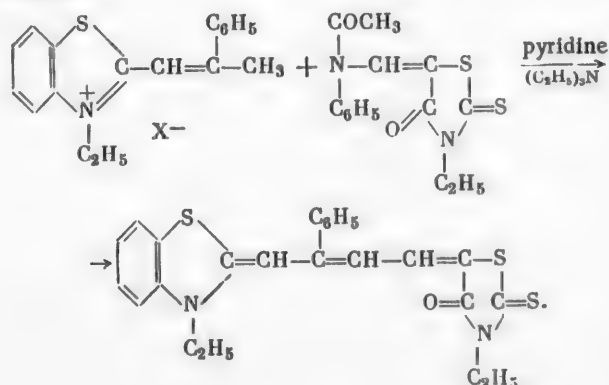


TABLE 3

Benzo- and Dibenzothiacarbocyanines

Substance No.	General formula	R	Absorption maximum (in mμ)	Displacement of absorption maximum (in mμ) relative to B
B		H	594	—
XVII		C ₆ H ₅	595	+ 1
XVIII			610	+16
—		H	578	—
XIX		C ₆ H ₅	580	+ 2
XX			594	+16
XXI			598	+20
XXII			602	+24
—		H	581	—
XXIII			595	+14
—		H	596	—
XXIV			610	+14

Even in 1949 [1], we condensed various aromatic ketones with quaternary salts of 2-methylbenzthiazole and thus obtained a series of quaternary salts of β -aryl substituted 2-propenylbenzthiazole. Later [2] several mesoarylthiacarbocyanines were obtained from β -aryl substituted 2-propenylbenzthiazoles and quaternary salts of 2-methylmercaptobenzthiazole. In 1957 a patent abstract was published [10] in which β -aryl substituted 2-propenylbenzthiazoles and their condensation with quaternary salts of 2-methylmercaptobenzthiazole and 2-acetanilidovinylbenzthiazole were described. Thus, we had synthesized quaternary salts of β -substituted 2-propenylbenzthiazole and converted the latter into meso substituted thiacarbocyanines considerably earlier.

EXPERIMENTAL

p-Hydroxyacetophenone [11], o-hydroxyacetophenone [11], o-methoxyacetophenone [12], p-acetylaminoacetophenone [13], p-nitroacetophenone [14], p-methoxyacetophenone [15], α -acetylnaphthalene [16], α -acetylthiophene [17], α -acetylcoumarone [18], methyl 2-benzthiazolyl ketone [19], p-dimethylaminoacetophenone [20], and α -acetylfuran were prepared according to literature data.

General procedure for condensing ketones with the ethyl-p-toluenesulfonate of 2-methylbenzthiazole. A mixture of ketone, quaternary salt, and acetic anhydride was heated on an oil bath for 10-15 hours at 140-200° (in the oil). To the cooled mass was added 100-200 ml of ether and the mixture carefully stirred to remove acetic anhydride and unreacted ketone. After 5-6 hours the ether was decanted and the dark, viscous mass again treated with 80-150 ml of ether as described above. The viscous mass was then dissolved in methanol and to the

TABLE 4

Quaternary Salts of β -Substituted 2-Propenylbenzthiazoles

Substance No.	Name of β -substituted 2-propenylbenzthiazole	Amount of ethyl-p-toluenesulfonate of 2-methylbenzthiazole or 2-methyl-benzobenzthiazole (in g)	Ketone and amount of it (in g)	Amount of acetic anhydride (in ml)	Oil bath temperature	Heating time (in hours)	Yield (in %)	Melting point
XXV	Iodoethylate of 2- β -phenyl-propenylbenzthiazole	5.2	Acetophenone (12)	6	155-165°	12	22	179-181°
XXVI	Ethyl-p-toluenesulfonate of 2- β -(p-methoxyphenyl)-propenylbenzthiazole	17.2	p-Methoxyacetophenone (15)	15	Boiling	6	20	171-172
XXVII	Iodoethylate of 2- β -(p-dimethylaminophenyl)-propenylbenzthiazole	3.4	p-Dimethylaminoacetophenone (1.6)	6	Boiling	2	33	210-211
XXVIII	Ethyl-p-toluenesulfonate of 2- β -(α -thienyl)-propenylbenzthiazole	10.4	α -Acetylthiophene (9.4)	10	155-160	12	29	186-187
XXIX	Ethyl-p-toluenesulfonate of 2- β -(α -furyl)-propenylbenzthiazole	6.9	α -Acetylfuran (11)	10	150-155	12	20	187
XXX	Iodoethylate of 2- β -(α -benzofuryl)-propenylbenzthiazole	10.4	α -Acetylcoumarone (9.6)	10	160-165	10	31	206-207
XXXI	Iodoethylate of 2- β -(p-acetylaminophenyl)-propenylbenzthiazole	10.4	p-Acetylaminacetophenone (17.7)	20	155-165	12	34	218
XXXII	Iodoethylate of 2- β -(p-hydroxyphenyl)-propenylbenzthiazole	3.4	p-Hydroxyacetophenone (4)	7	155-160	11	49	211
XXXIII	Ethyl-p-toluenesulfonate of 2- β -(p-nitrophenyl)-propenylbenzthiazole	5.2	p-Nitroacetophenone (8.2)	10	150-155	12	40	197
XXXIV	Iodoethylate of 2- β -(o-methoxyphenyl)-propenylbenzthiazole	10.5	o-Methoxyacetophenone (15)	10	155-160	12	45	-

TABLE 4 (continued)

Substance No.	Name of β -substituted 2-propenylbenzthiazole	Amount of ethyl-p-toluenesulfonate of 2-methylbenzthiazole or 2-methylbenzobenzthiazole (in g)	Ketone and amount of it (in g)	Amount of acetic anhydride (in ml)	Oil bath temperature	Heating time (in hours)	Yield (in %)	Melting point
XXXV	Iodoethylate of 2- β -(α -naphthyl)-propenylbenzthiazole	6.9	α -Acetylnaphthalene (8.5)	6	155-160°	12	10	142-144°
XXXVI	Ethylperchlorate of 2- β -[benzthiazolyl-(2)]-propenylbenzthiazole	6	Methyl-2-benzthiazolyl ketone (6.6)	10	180-185	6	4	168-170
XXXVII	Iodoethylate of 2- β -(p-methoxyphenyl)-propenyl-4,5-benzobenzthiazole	3.9	p-Methoxyacetophenone (6.5)	5	150-160	15	37	196
XXXVIII	Ethyl-p-toluenesulfonate of 2- β -(α -thienyl)-propenyl-6,7-benzobenzthiazole	7.9	α -Acetylthiophene (3.4)	7	155-160	12	35	-
XXXIX	Ethyl-p-toluenesulfonate of 2- β -(α -thienyl)-propenyl-4,5-benzobenzthiazole	3.9	α -Acetylthiophene (6.5)	5	150-155	12	21	-
XL	Iodoethylate of 2- β -(α -furyl)-propenyl-6,7-benzobenzthiazole	11.9	α -Acetylfuran (16.5)	10	150-160	12	30	233
XLI	Ethyl-p-toluenesulfonate of 2- β -(α -benzofuryl)-propenyl-6,7-benzobenzthiazole	19.9	α -Acetylcoumarone (16)	15	160-165	13	51	218

TABLE 5

9-Substituted Thiacyanocyanines

Dye No.	Dye name	Propenyl derivative and amount taken (in g)	Amount of iodoethylate of 2-methyl-mercaptobenzthiazole (in g)	Triethylamine (in ml)	Yield (in %)	Melting point	Found		Empirical formula	Calculated	
							element	content (in %)		element	content (in %)
I	3,3'-Diethyl-9-phenylthiacyanocyanine iodide	XXV (0.81)	0.67	0.7	63	281°	I	22.24, 22.13	$C_{17}H_{15}N_2S_2I$	I	22.35
II	3,3'-Diethyl-9-(p-dimethylaminophenyl)-thiacyanocyanine iodide	XXVII (1.35)	1	1	42	274	I	22.16, 20.69	$C_{21}H_{21}N_4S_2I$	I	20.78
III	3,3'-Diethyl-9-(p-methoxyphenyl)-thiacyanocyanine iodide	XXVI (0.48)	0.33	0.5	57	275	I	21.82, 21.83	$C_{21}H_{19}ON_2S_2I$	I	21.23
IV	3,3'-Diethyl-9-(o-methoxyphenyl)-thiacyanocyanine iodide	XXXIV (5.7)	4.4	2.5	40	266-267	I	21.13, 21.06	$C_{21}H_{17}ON_2S_2I$	I	21.23
V	3,3'-Diethyl-9-(p-acetylaminophenyl)-thiacyanocyanine iodide	XXXI (1.38)	1.01	0.6	45	290	I	20.46, 20.74	$C_{21}H_{15}ON_2S_2I$	I	20.32
XI	3,3'-Diethyl-9-(α -naphthyl)-thiacyanocyanine iodide	XXXV (0.5)	0.37	0.5	38	286-287	I	20.28, 20.49	$C_{27}H_{21}N_2S_2I$	I	20.55
XII	3,3'-Diethyl-9-(p-nitrophenyl)-thiacyanocyanine iodide	XXXIII (0.49)	0.33	0.5	40	275-276	I	20.73, 20.50	$C_{27}H_{17}N_3O_2S_2I$	I	20.71
XIII	3,3'-Diethyl-9-(α -thienyl)-thiacyanocyanine iodide	XXVIII (0.45)	0.33	0.5	53	268	S	17.03, 17.13	$C_{25}H_{19}N_2S_2I$	S	16.72
XIV	3,3'-Diethyl-9-(α -furyl)-thiacyanocyanine iodide	XXIX (0.39)	0.33	0.4	20	245	I	22.76, 22.64	$C_{25}H_{17}ON_2S_2I$	I	22.75
XV	3,3'-Diethyl-9-(α -benzofuryl)-thiacyanocyanine iodide	XXX (1.3)	1	0.8	75	237	I	21.29, 21.25	$C_{29}H_{21}ON_2S_2I$	I	20.88
XVI	3,3'-Diethyl-9-[benzothiazolyl-(2)]-thiacyanocyanine perchlorate	XXXVI (0.4)	0.4	0.3	—	175	—	—	—	—	—

TABLE 5 (continued)

Dye No.	Dye name	Propenyl derivative and amount taken (in g)	Amount of iodoethylate of 2-methylmercaptobenzthiazole (in g)	Triethylamine (in ml)	Yield (in %)	Melting point	Found		Empirical formula	Calculated	
							element	content (in %)		element	content (in %)
XVII	3,3'-Diethyl-9-phenyl-6,7,6',7'-dibenzothiacarboxyanine bromide	XLII (0.5)	0.43*	0.4	35	289	Br	12.70, 12.76	$C_{35}H_{29}N_2S_2Br$	Br	12.88
XVIII	3,3'-Diethyl-9-(α -thienyl)-6,7,6',7'-dibenzothiacarboxyanine bromide	XXXVIII (0.5)	0.43*	0.5	22	302	Br	12.91, 13.20	$C_{35}H_{27}N_2S_2Br$	Br	12.75
XIX	[3-Ethyl-6,7-benzobenzthiazole-(2)]-[3-ethylbenzthiazole-(2)]-9-phenylthiacarboxyanine bromide	XLII (3)	2.2	0.7	36	288	Br	13.78, 13.64	$C_{31}H_{27}N_2S_2Br$	Br	14.01
XX	[3-Ethyl-6,7-benzobenzthiazole-(2)]-[3-ethylbenzthiazole-(2)]-9- α -thienylthiacarboxyanine iodide	XXVIII (0.45)	0.43*	0.5	56	266	I	20.35, 20.13	$C_{29}H_{25}N_2S_2I$	I	20.35
XXI	[3-Ethyl-6,7-benzobenzthiazole-(2)]-[3-ethylbenzthiazole-(2)]-9- α -furylthiacarboxyanine iodide	XL (1.34)	1	0.8	35	261	I	21.22, 21.36	$C_{29}H_{25}ON_2S_2I$	I	20.88
XXII	[3-Ethyl-6,7-benzobenzthiazole-(2)]-[3-ethylbenzthiazole-(2)]-9- α -benzofurylthiacarboxyanine bromide	XLI (1.08)	0.76	1.0	53	219	Br	12.84, 13.10	$C_{33}H_{27}ON_2S_2Br$	Br	12.44
XXIII	[3-Ethyl-4,5-benzobenzthiazole-(2)]-[3-ethylbenzthiazole-(2)]-9- α -thienylthiacarboxyanine iodide	XXXIX (1.52)	1	0.5	23	251	I	20.66, 20.78	$C_{29}H_{25}N_2S_2I$	I	20.35
XXIV	[3-Ethyl-6,7-benzobenzthiazole-(2)]-[3-ethyl-4,5-benzobenzthiazole-(2)]-9- α -thienylthiacarboxyanine bromide	XXXIX (1.52)	1.29	0.5	16	232	Br	12.75, 12.65	$C_{33}H_{27}N_2S_2Br$	Br	12.75

* The ethyl-p-toluenesulfonate of 2-methylmercapto-6,7-benzobenzthiazole was used.

hot alcohol solution was added an equal volume of water (to the appearance of turbidity) and 1-2 g of animal charcoal and the solution boiled, filtered, and evaporated on a water bath. To remove the original quaternary salt, we mixed the residue with a small amount of water and collected it by filtration. If a noncrystalline mass was obtained, it was dissolved in a small amount of methanol and the iodide or the perchlorate precipitated, collected, and recrystallized.

In some cases, after condensation the quaternary salts were extracted with a large amount of boiling water. The aqueous solution was evaporated to small volume and the quaternary salt of the propenyl derivative precipitated with potassium iodide. Table 4 gives the conditions for synthesizing quaternary salts of β -substituted 2-propenylbenzthiazoles and their yields.

Ethyl-p-toluenesulfonate of 2- β -phenylpropenyl-6,7-benzobenzthiazole (XLII). A mixture of 11.9 g of the ethyl-p-toluenesulfonate of 2-methyl-6,7-benzobenzthiazole, 15 g of acetophenone, and 10 ml of acetic anhydride was heated for 10 hours at 155-165° and 4 hours at 175-180°. After the usual treatment with ether, the residue was dissolved in 600 ml of boiling water (in 3 portions) and the hot aqueous solution decanted from the black, viscous mass and cooled. The yellow-orange oil which separated from the aqueous solution was collected, dissolved in a water-alcohol mixture and the solution boiled with animal charcoal and evaporated on a water bath. The dark mass was mixed with a small amount of acetone and the residue collected by filtration. The yield was 3.7 g (24%). The fine yellow-orange crystals had m. p. 153-154°. Evaporation of the aqueous solution yielded a mixture of the ethyl-p-toluenesulfonate of 2-methyl-6,7-benzobenzthiazole and the propenyl derivative.

Dyes. General procedure for the preparation of meso-substituted thiacyanines. Hot solutions of quaternary salts of β -substituted 2-propenylbenzthiazoles and 2-methylmercaptobenzthiazole in anhydrous alcohol were mixed and triethylamine added to the solution. The mixture was heated for 20-30 minutes on a boiling water bath. The dye formed immediately and usually precipitated in a crystalline state. It was collected by filtration and recrystallized from alcohol to constant melting point. The dyes were usually obtained as lustrous, coarse crystals of a green or blue-green color. If ethyl-p-toluenesulfonates of β -substituted 2-propenylbenzthiazoles were used for the condensation, the dye was precipitated with water and the precipitate dissolved in boiling alcohol; the dye was precipitated by the addition of a 10% aqueous solution of potassium iodide and then it was recrystallized from alcohol.

Before analysis, the dyes were dried in vacuum at 100-105°. Table 5 gives the conditions for synthesizing the dyes and the analysis results.

3,3'-Diethyl-9-(p-aminophenyl)-thiacyanine iodide (VI). A mixture of 0.2 g of dye (V), 5 ml of glacial acetic acid, and 2.5 ml of sulfuric acid (d 1.84) was heated on a paraffin bath for 1 hour at 120°. The mixture was poured into an aqueous solution of potassium iodide and the precipitate collected, washed with 10% ammonia solution and then water, and recrystallized from alcohol. The yield was 0.05 g (25%). The fine, dark green crystals had m. p. 228-229° (with decomp.).

Found %: I 20.65, 20.67. $C_{27}H_{26}N_3S_2I \cdot 2H_2O$. Calculated %: I 20.51.

3,3'-Diethyl-9-(p-hydroxyphenyl)-thiacyanine iodide (VII). The iodoethylate of 2- β -(p-hydroxyphenyl)-propenylbenzthiazole (2.1 g) and 1.68 g of the iodoethylate of 2-methylmercaptobenzthiazole were dissolved in 80 ml of anhydrous alcohol and 2 ml of triethylamine added to the solution. The mixture was boiled on a water bath for 40 minutes. Simultaneously with the formation of the thiacyanine, HI was eliminated and the hydroxystyryl base with a methyl group in the β -position formed. The precipitate was recrystallized four times from alcohol. The yield was 0.4 g (13%). The green tablets had m. p. 299-301° (with decomp.). This dye was obtained much more readily by demethylation of 3,3'-diethyl-9-(p-methoxyphenyl)-thiacyanine iodide (III). A mixture of 0.7 g of dye (III) and 2.5 ml of hydrobromic acid (d 1.76, 66%) was heated in a sealed tube for 7 hours at 150-155°. The cooled contents of the tube were poured into 60 ml of water. The precipitate was collected, washed with water, dissolved in boiling alcohol, filtered, and to the hot alcohol solution was added an aqueous solution of potassium iodide. The precipitated dye was collected and washed with warm water, methanol, and ether. The yield was 0.4 g (58%). The lustrous green tablets had m. p. 299-301° (with decomp.).

Found %: I 21.63, 21.72. $C_{27}H_{26}ON_2S_2I$. Calculated %: I 21.74.

The melting point of a mixture of the dyes obtained by the first and second methods was not depressed.

3,3'-Diethyl-9-(o-hydroxyphenyl)-thiacarbocyanine iodide (IX): Thiacarbocyanine (IV) (1.5 g) was demethylated and purified as described above. The yield was 0.95 g (67%). The green crystals had m. p. 257° (with decomp.).

Found %: I 22.17, 22.23. $C_{27}H_{25}ON_2S_2I$. Calculated %: I 21.74.

3-Ethyl-5-(3'-ethylbenzthiazolinyldene-2'- β -phenylbutenyldene)-thiazolidinethion-(2)-one-(4). To a solution of 0.8 g of the iodoethylate of 2- β -phenylpropenylbenzthiazole and 0.6 g of 3-ethyl-5-(acetanilidomethylene)-rhodanine in 8 ml of dry pyridine was added 0.4 ml of triethylamine. The mixture was boiled for 15 minutes and the merocyanine precipitated with water, collected by filtration, washed with warm water, and purified in the following way. The dye was dissolved in the minimal amount of pyridine with heating and filtered and to the hot pyridine solution was added five times the volume of methyl alcohol. The mixture was heated to boiling and left to crystallize. The precipitate was collected by filtration and washed with water and methanol. The yield was 0.4 g (46%). The lustrous green tablets had m. p. 210-211°. λ_{max} 633 m μ .

Found %: N 6.25, 6.35; S 21.08, 20.95. $C_{24}H_{22}ON_2S_3$. Calculated %: N 6.22; S 21.33.

3,3'-Diethyl-9-phenylthiadcarbocyanine iodide. A mixture of 0.5 g of the iodoethylate of 2- β -phenylpropenylbenzthiazole, 0.5 g of the iodoethylate of 2-acetanilidovinylbenzthiazole, 7 ml of anhydrous alcohol, and 0.5 ml of triethylamine was boiled for 20 minutes. The solution was diluted with water and the precipitate collected and recrystallized twice from alcohol. The yield was 0.25 g (35%). The green crystals had m. p. 189-190° and λ_{max} 668 m μ . The melting point of a mixture with 9-phenylthiadcarbocyanine obtained by the method in [9] was not depressed.

2-[4'-(p-Dimethylaminophenyl)-2'-phenyl-1',3'-butadien-1'-yl]-3-ethylbenzthiazolium iodide. A mixture of 0.4 g of the iodoethylate of 2- β -phenylpropenylbenzthiazole, 0.14 g of p-dimethylaminobenzaldehyde, and 2 ml of acetic anhydride was boiled for 30 minutes. The dye was precipitated with water, collected, and recrystallized from alcohol. The yield was 0.18 g (34%). The dark green, lustrous needles had m. p. 219° and λ_{max} 580 m μ .

Found %: N 4.98, 5.06. $C_{27}H_{27}N_2SI$. Calculated %: N 5.20.

3-Ethyl-5-(3'-ethyl-6,7-benzobenzthiazolinyldene-2'- β -phenylbutenyldene)-thiazolidinethion-(2)-one-(4). The ethyl-p-toluenesulfonate of 2- β -phenylpropenyl-6,7-benzobenzthiazole (3.9 g) was dissolved in 20 ml of pyridine. To a solution was added 2.4 g of 3-ethyl-5-(acetanilidomethylene)-rhodanine and 2 ml of triethylamine and the mixture boiled for 35 minutes. The reaction mixture was poured into water and the precipitate ground with water in a mortar, collected by filtration, dried, dissolved in chloroform, and chromatographed on aluminum oxide twice. The merocyanine was finally recrystallized from a mixture of pyridine and methanol as indicated above. The shiny crystals with a bronze luster had m. p. 236-237°. The yield was 0.7 g (18%) and λ_{max} 651 m μ .

Found %: N 5.88, 5.90; S 19.00, 19.03. $C_{28}H_{24}ON_2S$. Calculated %: N 5.60; S 19.20.

SUMMARY

1. Quaternary salts of 2-methylbenzthiazole were condensed with various aromatic and heterocyclic ketones to give a series of quaternary salts of β -substituted 2-propenylbenzthiazoles.

2. From the quaternary salts of β -substituted 2-propenylbenzthiazoles and the iodoethylate of 2-methylmercaptobenzthiazole we synthesized a series of thiacarbocyanines containing various aromatic and heterocyclic radicals in the meso position.

3. It was established that the introduction of various aryl radicals into Position 9 of thiacarbocyanine had hardly any effect on the absorption. The introduction of heterocyclic radicals into the meso position of thiacarbocyanine produced a considerable bathochromic effect.

4. It was shown that quaternary salts of 2- β -arylpropenylbenzthiazoles condense with 3-ethyl-5-(acetanilidomethylene)-rhodanine, the iodoethylate of 2-acetanilidovinylbenzthiazole, and p-dimethylaminobenzaldehyde to form tetramethynemerocyanines, 9-aryl substituted thiacarbocyanines, and styryl dyes.

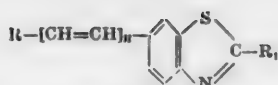
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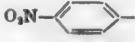
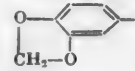
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* Original Russian pagination. See C. B. Translation.

TABLE 1

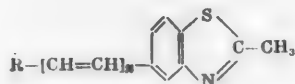


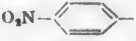
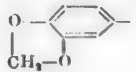
Compound No.	R	R ₁	n	Yield (in %)	Melting point
I		CH ₃	1	4.7	179—180°
II		CH ₃	1	10.4	165—166
III	C ₆ H ₅	C ₂ H ₅	1	14.3	120—121
IV	CH ₃	CH ₃	2	10	38—39
V	C ₆ H ₅	CH ₃	2	14.6	156—157
VI	C ₆ H ₅	C ₂ H ₅	2	15.4	161—162

acetone and also the occurrence of a number of side processes (Sandmeyer reaction and the formation of azo compounds and "azo resins"). The bases readily formed picrates and also quaternary salts under the action of alkylating agents.

For the preparation of thiacyanines, the quaternary salts were condensed with orthoesters of carboxylic acids in pyridine with the addition of small amounts of acetic anhydride and in this case the quaternary salts of 2-methyl-5- or 6-butadienylbenzthiazoles condensed only with orthoformic ester.

TABLE 2



Compound No.	R	n	Yield (in %)	Melting point
VII		1	2.2	173—174°
VIII		1	9.5	125—126
IX	C ₆ H ₅	2	8.7	158—160°

The absorption maxima (in mμ) of the thiacyanines synthesized are given in Table 3. The introduction of unsaturated groupings into positions 5,5' and 6,6' strongly displaced the absorption maximum into the longwave region of the spectrum; a greater bathochromic effect was observed for thiacyanines with unsaturated groupings in the 6,6'-positions than for the corresponding 5,5'-derivatives. Thus, for 5,5'-distyrylthiacyanine the displacement of the absorption maximum into the longwave region in comparison with the unsubstituted dye was 20 mμ, while for the corresponding 6,6'-derivative it was 37 mμ.

With the lengthening of the conjugation chain by yet another vinylene group, as in the case of both 5,5'- and 6,6'-derivatives, there was a further deepening in color, reaching +53 mμ.

The 5,5'- and 6,6'-distyrylthiacyanines behaved differently when electron-donor and electron-acceptor groups were introduced into the para position of the styryl radical. Such electropositive groups as methyl and

methoxy deepened the color of both 5,5'- and 6,6'-derivatives. However, when nitro groups were introduced into 5,5'-distyrylthiacarbocyanines the color hardly changed, while in the case of 6,6'-derivatives, there was a deepening in color.

TABLE 3

Compound No.	R.	Position of substituents			
		5,5'-		6,6'-	
		λ_{\max} (in m μ)	$\Delta\lambda_{\max}$	λ_{\max} (in m μ)	$\Delta\lambda_{\max}$
X	$\text{CH}_3\text{---}[\text{CH}=\text{CH}]_2\text{---}$	—	—	589	+31
XI—XII	$\text{C}_6\text{H}_5\text{---}[\text{CH}=\text{CH}]_2\text{---}$	592	+34	611	+53
XIII—XIV	$\text{O}_2\text{N---}\langle\text{---}\rangle\text{---CH}=\text{CH---}$	576	+18	601	+43
XV—XV	$\text{O---}\langle\text{---}\rangle\text{---CH}=\text{CH---}$ $\text{CH}_2\text{---O}$	567	+9	602	+44

The data presented agree with the rules established previously for thiacarbocyanines containing electro-negative [6] and electropositive [5] substituents directly in the 5,5'- and 6,6'-positions of the benzthiazole nucleus; moreover, as in the case of the dyes examined here, the effect of these groups on the color was weakened. When styryl groups were replaced by β -2'-thienylvinyl groups there was a bathochromic displacement, while

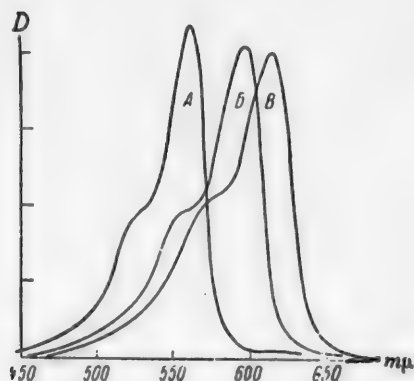
TABLE 4

Compound No.	B	Position of substituents			
		5,5'-		6,6'-	
		λ_{\max} (in m μ)	$\Delta\lambda_{\max}$	λ_{\max} (in m μ)	$\Delta\lambda_{\max}$
XVII, XVIII	$\text{C}_6\text{H}_5\text{---CH}=\text{CH---}$	666	+13	686	+33
XIX, XX	$\text{CH}_3\text{O---}\langle\text{---}\rangle\text{---CH}=\text{CH---}$	670	+17	696	+43
XXI, XXII	$\langle\text{---}\rangle\text{---CH}=\text{CH---}$ S	670	+17	696	+43

replacement of coumarinyl groups produced a heightening in color. The high color of 5,5'-bis(piperonylvinyl)-thiacarbocyanine was unexpected.

The figure shows absorption curves of 3,3'-diethyl- (A), 3,3'-diethyl-6,6'-distyryl- (B), and 3,3'-diethyl-6,6'-di-(γ -phenylbutadienyl)-thiacarbocyanines (c).

The absorption curves of thiadibocyanines containing unsaturated groupings in the 6,6'-positions were of the same form and hardly differed in character from that of 3,3'-diethylthiadibocyanine (A). When unsaturated groupings were introduced into the 6,6'-positions of thiadibocyanine, the absorption maxima were strongly displaced toward longer wavelengths. The absorption curves and maxima of dyes presented indicate that unsaturated radicals in the 5,5'- and 6,6'-positions of thiadibocyanine are in conjugation with the polymethyne chain and form a single, considerably lengthened chromophore.



Absorption curves of 3,3'-diethyl- (A), 3,3'-diethyl-6,6'-distyryl- (B) and 3,3'-diethyl-6,6'-di-(γ -phenylbutadienyl)-thiadibocyanines (C).

By condensing the quaternary salts of bases obtained previously [1, 2] with the dianil of methylmalonic aldehyde in a pyridine medium, we synthesized six thiadibocyanines which are listed in Table 4.

The introduction of *p*-methoxystyryl or thienylvinyl groups into the 6,6'-positions of 10-methylthiadibocyanine displaced the absorption maximum of the dye to almost 700 m μ .

EXPERIMENTAL

Styrylacrylic [7] and sorbic [8] acids were prepared according to literature data.

Synthesis of Bases and Quaternary Salts

The general procedure for synthesizing, isolating, and purifying 2-methylbenzthiazoles with unsaturated groupings in Position 5 or 6 were given in our previous communication [2].

2-Methyl-6-*p*-nitrostyrylbenzthiazole (I). In a three-necked flask were mixed 9.6 g of *p*-nitrocinnamic acid, 200 ml of acetone, 13.6 g of crystalline sodium acetate, and 2.5 g of cupric chloride in 10 ml of water. The mixture was cooled to -3° and to it was added the diazonium chloride prepared from 8.2 g of 2-methyl-6-aminobenzthiazole, 12.5 ml of hydrochloric acid (d 1.19), 10 ml of water, and 3.7 g of sodium nitrite in 6 ml of water. After chromatographic purification, the precipitate was recrystallized from 40 ml of alcohol. The yield was 0.7 g (4.7%). The yellow plates had m. p. $179-180^{\circ}$.

Found %: N 9.40, 9.46. $C_{16}H_{12}O_2N_2S$. Calculated %: N 9.45.

The picrate formed yellow plates with m. p. $198-200^{\circ}$.

Found %: N 13.25, 13.20. $C_{22}H_{15}O_3N_5S$. Calculated %: N 13.32.

2-Methyl-6-(8-piperonylvinyl)-benzthiazole (II). This compound was obtained analogously from 9.6 g of piperonylacrylic acid and 8.2 g of 2-methyl-6-aminobenzthiazole. The yield was 1.54 g (10.4%). The light yellow needles had m.p. $165-166^{\circ}$ (from alcohol).

Found %: S 10.86, 10.76. $C_{17}H_{15}O_2NS$. Calculated %: S 10.83.

The picrate formed yellow plates with m. p. $185-186^{\circ}$ (from alcohol).

Found %: N 10.47, 10.52. $C_{23}H_{16}O_3N_4S$. Calculated %: N 10.65.

2-Ethyl-6-styrylbenzthiazole (III). 17.8 g of 2-ethyl-6-aminobenzthiazole was diazotized by the usual method. Into a flask were placed 14.8 g of cinnamic acid, 150 ml of acetone, 27 g of sodium acetate, and 5.2 g of cupric chloride in 12 ml of water and the mixture cooled to -4° . To the mixture was added the cooled diazonium chloride. The mixture was stirred at 0° for 2 hours and at room temperature for 4 hours. A large amount of carbon dioxide was liberated. The base was treated and purified as described above. The yield was 3.8 g (14.3%). The lustrous colorless plates had m. p. $120-121^{\circ}$ (from alcohol).

Found %: S 12.33, 12.38. $C_{17}H_{15}NS$. Calculated %: S 12.07.

2-Methyl-6-(4'-methylbutadienyl-1')-benzthiazole (IV). This compound was obtained from 16.4 g of 2-methyl-6-aminobenzthiazole and 11.2 g of sorbic acid in 120 ml of acetone. The mixture was purified

TABLE 5

Compound No.	Name of dye	Amount taken					Yield (in %)	Melting point	N found, %	Empirical formula	N. calculated, %
		base (g)	alkylating agent (g)*	second component (g)**	pyridine (ml)	piperidine (ml)					
XI	3,3'-Diethyl-5,5'-di-(4'-phenylbutadienyl-1')-thiacarbocyanine bromide	0.27	E-0.22	I-0.5	3.5	-	48	210-212°	3.77, 3.70	C ₄₁ H ₃₇ N ₂ S ₂ Br	3.99
XIII	3,3'-Diethyl-5,5'-di-p-nitrostyryl-thiacarbocyanine ethylsulfate	0.29	D-0.16	I-0.5	3	-	46	294-295	2.68, 6.83	C ₃₈ H ₃₅ O ₂ N ₄ S ₂	7.13
XIV	3,3'-Diethyl-6,6'-di-p-nitrostyryl-thiacarbocyanine ethylsulfate	0.29	D-0.16	I-0.5	3	-	63	264-266	6.82, 6.97	C ₃₈ H ₃₅ O ₂ N ₄ S ₂	7.13
XV	3,3'-Diethyl-5,5'-di-β-(2'-piperonyl)-vinylthiacarbocyanine ethylsulfate	0.3	D-0.16	I-0.5	3	-	51	320	3.47, 3.59	C ₄₁ H ₃₈ O ₃ N ₄ S ₂	3.58
XVI	3,3'-Diethyl-6,6'-di-β-(2'-piperonyl)-vinylthiacarbocyanine ethylsulfate	0.3	D-0.16	I-0.5	3	-	64	260	3.83, 3.71	C ₄₁ H ₃₈ O ₃ N ₄ S ₂	3.58
XVII	3,3'-Diethyl-5,5'-distyryl-10-methylthiacarbocyanine p-toluenesulfonate	0.5	E-0.44	II-0.24	3.5	0.17	33	218-220	3.81, 3.71	C ₄₇ H ₄₄ O ₃ N ₂ S ₂	3.58
XVIII	3,3'-Diethyl-6,6'-distyryl-10-methylthiacarbocyanine bromide	0.5	E-0.44	II-0.24	3.5	0.17	76	220-221	3.91, 3.91	C ₄₀ H ₃₇ N ₂ S ₂ Br	4.10
XIX	3,3'-Diethyl-5,5'-di-p-methoxystyryl-10-methylthiacarbocyanine p-toluenesulfonate	0.56	E-0.44	II-0.24	3.5	0.17	59	243-244	3.74, 3.79	C ₄₈ H ₄₆ O ₃ N ₂ S ₂	3.32
XX	3,3'-Diethyl-6,6'-di-p-methoxystyryl-10-methylthiacarbocyanine p-toluenesulfonate	0.58	E-0.44	II-0.24	3.5	0.17	64	260	3.37, 3.42	C ₄₈ H ₄₆ O ₃ N ₂ S ₂	3.32
XXI	3,3'-Diethyl-5,5'-di-β-(2'-thienyl)-vinyl-10-methylthiacarbocyanine p-toluenesulfonate	0.52	E-0.44	II-0.24	3.5	0.17	34	232	3.61, 3.65	C ₄₈ H ₄₆ O ₃ N ₂ S ₂	3.50

* Diethyl sulfate - D; ethyl p-toluenesulfonate - E.

** Orthoformic ester - I; dianil of β-methylmalonic aldehyde - II.

after the addition of hydroquinone. An almost colorless oil was obtained and this crystallized after standing for three days. The yield was 4.3 g (20%) and the m. p. 37-38°. The base contained no halogen.

2-Methyl-6-(4'-phenylbutadienyl-1')-benzthiazole (V). 2-Methyl-6-aminobenzthiazole (16.4 g) was diazotized under the usual conditions. Into a flask were placed 160 ml of acetone, 17.4 g of styrylacrylic acid, 27.2 g of crystalline sodium acetate in 15 ml of water, and 5.1 g of cupric chloride in 5 ml of water. The mixture was cooled to -5° and the benzthiazole diazonium chloride added to it in one portion. Vigorous evolution of nitrogen and carbon dioxide began after 10-15 minutes. The reaction mixture was stirred at -2° for 3 hours and at room temperature for 4 hours. To the contents of the flask was added 0.1 g of hydroquinone and the mixture purified in the usual way. Benzene was used for elution and then the base was recrystallized from alcohol. The yield was 4 g (14.6%). The lustrous, light yellow plates had m. p. 156-157°. Solutions of the base fluoresced very strongly in sunlight.

Found %: S 11.51, 11.43. $C_{18}H_{15}NS$. Calculated %: S 11.55.

2-Ethyl-6-(4'-phenylbutadienyl-1')-benzthiazole (VI). This compound was obtained from 17.8 g of 2-ethyl-6-aminobenzthiazole and 17.4 g of styrylacrylic acid under the conditions of the Meerwein reaction. To the reaction mass was added 0.1 g of hydroquinone and the mixture steam distilled and then purified normally. Recrystallization from alcohol with treatment with animal charcoal yielded 4.5 g (15.4%) of product. The colorless, lustrous tablets had m. p. 161-162°.

Found %: S 11.01, 11.03. $C_{19}H_{17}NS$. Calculated %: S 10.99.

2-Methyl-5-p-nitrostyrylbenzthiazole (VII) was obtained similarly to base (I). Recrystallization from alcohol yielded 0.3 g (2.2%) of product. The yellow crystals had m. p. 173-174°.

Found %: N 9.37; 9.38. $C_{16}H_{12}O_2N_2S$. Calculated %: N 9.45.

2-Methyl-5-(β -piperonylvinyl)-benzthiazole (VIII) was obtained analogously to base (II). The preparation was recrystallized from 40 ml of alcohol. The colorless crystals had m. p. 125-126°. The yield was 1.4 g (9.5%).

Found %: S 10.93, 10.73. $C_{17}H_{13}O_2NS$. Calculated %: S 10.83.

The picrate formed yellow plates from alcohol with m. p. 193-194°.

Found %: N 10.59, 10.50. $C_{23}H_{16}O_9N_4S$. Calculated %: N 10.65.

2-Methyl-5-(γ -phenylbutadienyl)-benzthiazole (IX). This compound was obtained analogously to base (V) from 2-methyl-5-aminobenzthiazole and styrylacrylic acid. The yield was 4 g (14.4%). Recrystallization from ligroine (b.p. 90-120°) yielded 2.4 g (8.7%) of product. The yellow plates had m. p. 158-160°.

Found %: N 5.09, 5.11. $C_{18}H_{15}NS$. Calculated %: N 5.05.

Ethyl-p-toluenesulfonate of 2-methyl-6-(4'-phenylbutadienyl-1')-benzthiazole. A mixture of 2.7 g of 2-methyl-6-(4'-phenylbutadienyl-1')-benzthiazole, 3 g of ethyl p-toluenesulfonate, and 10 mg of hydroquinone was heated at 155-160° for 6 hours. The salt was dissolved in boiling water, the solution extracted with benzene, and the aqueous solution boiled with animal charcoal and evaporated on a water bath. The yield was 2.4 g (51%).

Ethyl-p-toluenesulfonate of 2-methyl-6-(4'-methylbutadienyl-1')-benzthiazole. A mixture of 4.3 g of 2-methyl-6-(4'-methylbutadienyl-1')-benzthiazole, 6 g of ethyl p-toluenesulfonate, and 20 mg of hydroquinone was heated at 155-160° for 7 hours. The yield was 5.3 g (63%).

Synthesis of Dyes

For the preparation of thiadibocyanines, appropriate bases were heated in a flask with a reflux condenser on a paraffin bath with 10-15% excess of diethyl sulfate at 140-150° for 4-5 hours. To the solid mass of quaternary salt were added orthoformic ester and dry pyridine. The mixture was boiled for 25-30 minutes. The dye was precipitated with ether and recrystallized from alcohol. The dyes formed violet crystals.

Thiadibocyanines were obtained by heating ethyl-p-toluenesulfonates of appropriate bases with the dianil of β -methylmalonic aldehyde in dry pyridine in the presence of piperidine. The dye was precipitated from the cooled solution with ether. The dye was washed several times with ether and then with a small amount

of alcohol and recrystallized from alcohol. The dyes usually precipitated in the form of green crystals. Table 5 gives the synthesis conditions and the analysis results for the dyes.

3,3'-Diethyl-6,6'-(4'-methylbutadienyl-1')-thiacarbocyanine iodide (X). To a solution of 0.41 g of the ethyl-p-toluenesulfonate of 2-methyl-6-(4'-methylbutadienyl-1')-benzthiazole and 2.5 ml of pyridine were added 0.4 g of orthoformic ester and 6 drops of acetic anhydride and the mixture boiled for 25 minutes. The dye was precipitated with an aqueous solution of potassium iodide and recrystallized from a pyridine-alcohol mixture. The yield was 0.13 g (20%). The fine black crystals had m. p. 248-249° (with decomp.).

Found %: I 20.67, 20.50. $C_{31}H_{33}N_2S_2I$. Calculated %: I 20.35.

3,3'-Diethyl-6,6'-di-(4'-phenylbutadienyl-1')-thiacarbocyanine iodide (XII). The ethyl-p-toluenesulfonate of 2-methyl-6-(4'-phenylbutadienyl-1')-benzthiazole (0.89 g) was dissolved in 3 ml of pyridine.

To the solution were added 0.9 g of orthoformic ester and 6 drops of acetic anhydride, the mixture boiled for 30 minutes, and the dye precipitated with a hot aqueous solution of potassium iodide. On the following day the precipitate was collected, washed with water, dried, and recrystallized twice from a mixture of pyridine and alcohol. The yield was 0.37 g (25%). The fine, dark crystals had m. p. 232-233°.

Found %: I 16.92, 17.06. $C_{41}H_{37}N_2S_2I$. Calculated %: I 16.87.

Thiacarbocyanines containing butadienyl groupings in the benzthiazole nuclei readily decomposed during purification.

SUMMARY

1. Reaction of p-nitrocinnamic, piperonylacrylic, cinnamic, styrylacrylic, and sorbic acids with 2-methyl-5-, 3-methyl-6-, and 2-ethyl-6-benzthiazole diazonium chlorides yielded nine new benzthiazole derivatives with unsaturated radicals in positions 5 and 6 of the benzthiazole nucleus.
2. Condensation of quaternary salts of the new bases with orthoesters of carboxylic acids in pyridine yielded nine thiacarbocyanines.
3. Five thiadicarbocyanines were synthesized by condensation of quaternary salts of benzthiazoles containing unsaturated radicals with the dianil of methylmalonic aldehyde.
4. The optical properties of the dyes synthesized were investigated. It was established that the introduction of unsaturated substituents into the benzthiazole nuclei of thiacarbo- and thiadicarbocyanines produced a considerable bathochromic effect of up to 53 mμ.

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CYANINE DYES WITH UNSATURATED SUBSTITUENTS

IV. QUINOCYANINES WITH PHENYLBUTADIENYL AND STYRYL RADICALS IN THE QUINOLINE NUCLEUS

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In previous work [1, 2] we showed that the introduction of unsaturated groupings into the thiacyanine molecule strongly displaced the absorption maximum into the longwave region of the spectrum. In the present communication we report the synthesis of quinaldines containing styryl and phenylbutadienyl radicals as substituents and cyanine dyes synthesized from the quinaldines. The starting bases were synthesized by the Meerwein reaction [3] by reaction of quinaldinediazonium chlorides with cinnamic and styrylacrylic acids. The preparation of 6-styrylquinaldine, for example, may be illustrated by the following scheme.

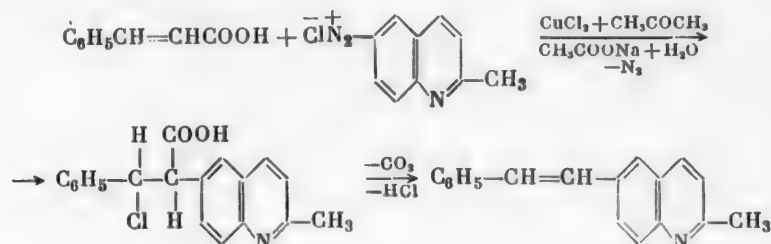
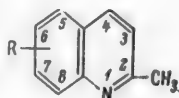


Table 1 lists the styryl- and phenylbutadienylquinaldines prepared.

TABLE 1

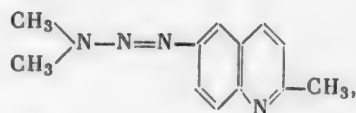


Compound No.	R	Position of substituent	Yield (in %)	Melting point
(I)	$\text{C}_6\text{H}_5\text{---CH}=\text{CH---}$	5	13	96--97°
(II)	$\text{C}_6\text{H}_5\text{---}[\text{CH}=\text{CH}]_2\text{---}$	5	15	129--130
(III)	$\text{C}_6\text{H}_5\text{---CH}=\text{CH---}$	6	21	155--156
(IV)	$\text{C}_6\text{H}_5\text{---}[\text{CH}=\text{CH}]_2\text{---}$	6	23	200--201

The yield of bases was quite low, as we also observed previously [1, 2]. The bases obtained did not dissolve in alkalis and did not contain chlorine, indicating complete dehalogenation and decarboxylation during the reaction. Benzene or chloroform solutions of the bases fluoresced very strongly in sunlight, added bromine, and decolorized potassium permanganate solution.

We were unable to synthesize 2-methyl-8-styrylquinoline by the reaction of diazotized 2-methyl-8-aminoquinoline with cinnamic acid (8-chloroquinaldine was obtained). Reaction of diazotized 6-aminoquinaldine with benzene in the presence of sodium acetate yielded 6-phenylquinaldine in 10% yield.

We previously established [4] that various arylbenzthiazoles could be obtained readily and in good yield through triazene derivatives of benzthiazoles. For this reason we used diazotized 6-aminoquinaldine to prepare the triazene:

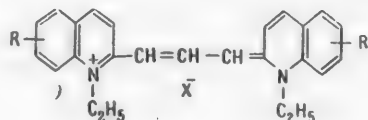


which, as subsequent experiments showed, did not form 6-phenylquinaldine when heated with benzene in the presence of glacial acetic acid. Only unreacted triazene was found in the reaction products.

The bases and 6-phenylquinaldine were converted into quaternary salts, which were condensed with orthoformic ester in pyridine. Dyes were not formed by condensation of the quaternary salts with orthoacetic and orthopropionic esters in the presence of various additives.

Table 2 gives the absorption maxima of the quinocarbocyanines with unsaturated radicals obtained.

TABLE 2



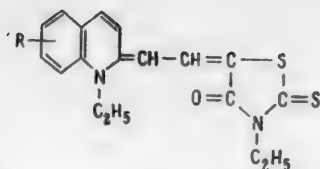
Compound No.	R	Position of substituent	Absorption maximum (in mμ)	Displacement of absorption max. (in mμ)
(V)	C ₆ H ₅ -CH=CH-	5	626 (580) *	+19
(VI)	C ₆ H ₅ -[CH=CH] ₂ -	5	631 (584)	+24
(VII)	C ₆ H ₅	6	625 (581)	+18
(VIII)	C ₆ H ₅ -CH=CH-	6	645 (596)	+38
(IX)	C ₆ H ₅ -[CH=CH] ₂ -	6	655 (605)	+48

* The first number is the main maximum and the second, an additional shortwave absorption maximum.

The introduction of unsaturated radicals into the quinocarbocyanine molecule produced quite a large displacement of the absorption maximum into the longwave part of the spectrum of up to 48 mμ. Quinocarbocyanines with styryl and phenylbutadienyl radicals in the 6,6'-positions were more deeply colored than the corresponding 5,5'-substituted derivatives. This can probably be explained by the fact that conjugation of unsaturated groupings in the 5,5'-positions with the polymethyne chromophore is considerably worse than in the case of 6,6'-derivatives as Position 5 in quinoline is a meta position relative to the nitrogen in the ring.

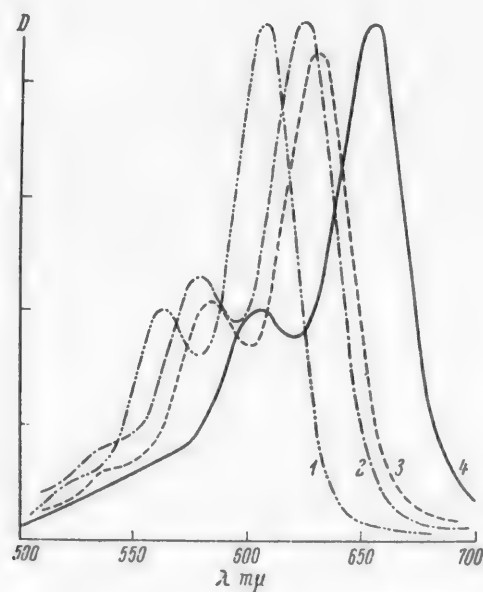
The introduction of phenyl, a weak electronegative substituent, into the 6,6'-positions of quinocarbocyanine produced a bathochromic effect equal to 18 mμ.

TABLE 3



Compound No.	R	Position of substituent	Absorption maximum (in mμ)	Displacement of absorption maximum (in Mμ)
—	H	—	568 (535)	—
(X)	C ₆ H ₅ -CH=CH-	5	578 (547)	+10
(XI)	C ₆ H ₅ -[CH=CH] ₂ -	5	585 (549)	+17
(XII)	C ₆ H ₅ -CH=CH-	6	584 (550)	+16
(XIII)	C ₆ H ₅ -[CH=CH] ₂ -	6	590 (552)	+22

Fig. 1 shows absorption curves of quinocarbocyanines containing styryl and phenylbutadienyl radicals.



Absorption curves of quinocarbocyanines containing styryl and phenylbutadienyl radicals. 1) 1,1'-Diethyl-quinocarbocyanine; 2) 1,1'-diethyl-5,5'-distyryl-quinocarbocyanine; 3) 1,1'-diethyl-5,5'-diphenyl-butadienylquinocarbocyanine; 4) 1,1'-diethyl-6,6'-diphenylbutadienylquinocarbocyanine.

The absorption curves of quinocarbocyanines with unsaturated groupings in the quinoline nucleus were of the same type and completely analogous in character to the absorption curve of pinacyanol. The only difference

was in the position of the absorption maxima, as we observed previously for thiocarbocyanines with unsaturated groupings in the 6,6'-positions [2].

It was found that quaternary salts of substituted quinaldines condensed readily with 3-ethyl-5-(acetanilido-methylene)-rhodanine in anhydrous alcohol in the presence of triethylamine to form dimethynemerocyanines. for example:

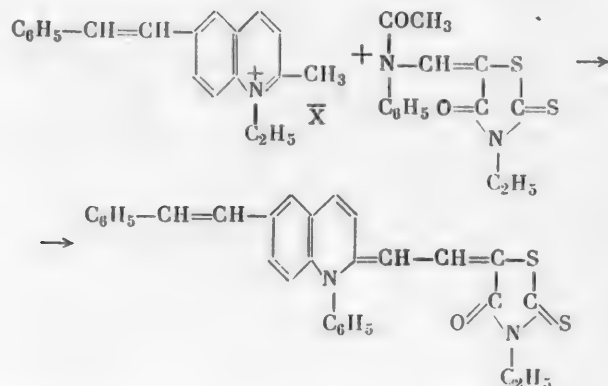


Table 3 gives the absorption maxima of the dimethynemerocyanines synthesized.

The introduction of unsaturated substituents into the quinoline nucleus of dimethynemerocyanine also produced a considerable bathochromic effect.

The absorption maxima of quinocarbocyanines and dimethynemerocyanines were determined in alcohol on an automatic recording SF-2M spectrophotometer.

EXPERIMENTAL

6-Aminoquinaldine was obtained by reduction of 6-nitroquinaldine [5].

5-Nitro- and 8-nitroquinaldines. With cooling to 5-10° and stirring, to 50 g of quinaldine was added 40 ml of concentrated sulfuric acid and then a nitrating mixture, consisting of 200 g (133 ml) of nitric acid (d 1.51) and 200 g (108 ml) of sulfuric acid (d 1.84). The mixture was heated to 60° on a water bath and after 20 minutes, poured into water. The nitroquinaldines were then separated according to literature data [6]. Methanol was used for recrystallization. The yield of 5-nitroquinaldine was 39 g (59%) and it had m. p. 82° and the yield of 8-nitroquinaldine with m. p. 137° was 22 g (33%).

5-Amino- and 8-aminoquinaldines were obtained by reduction of nitroquinaldines with tin in hydrochloric acid [6].

6-Phenylquinaldine. 6-Aminoquinaldine (4.7 g) was dissolved in 10 ml of hydrochloric acid (d 1.19) and 7 ml of water. The solution was cooled to -10° and diazotized with 2.2 g of sodium nitrite in 4 ml of water. After standing for 5 minutes at -5 to -7°, the diazonium chloride was added to 200 ml of benzene, cooled to +6°, and then a solution of 14 g of sodium acetate in 40 ml of water added with vigorous stirring. Stirring was continued for 3 hours at 7-8° and for 10 hours at 20°. The reaction mixture was filtered, the benzene layer separated, the aqueous one extracted with benzene, the benzene removed by distillation, and the residue dissolved in chloroform and chromatographed on aluminum oxide. The benzene was distilled from the eluate. The residue was a viscous oil which crystallized on standing. The yield was 0.68 g (11%). After recrystallization from ligroline, the product had m. p. 94-95°. The picrate crystallized from alcohol as lustrous yellow plates with m. p. 200°.

Found %: N 12.62, 12.70. $\text{C}_{22}\text{H}_{16}\text{O}_7\text{N}_4$. Calculated %: N 12.50.

2-Methylquinoly1-6-dimethyltriazene. 6-Aminoquinaldine (7.9 g) was dissolved in 12 ml of hydrochloric acid (d 1.19) and 10 ml of water. The solution was cooled to -5° and diazotized with 3.6 g of sodium nitrite in 7 ml of water. The diazonium chloride was then introduced dropwise into a cooled solution of 14 g of anhydrous sodium carbonate in 80 ml of water and 5.5 g (33%) of a solution of dimethylamine in anhydrous alcohol. The

brown lumps were ground up, collected by filtration, dried, and recrystallized from ligroine. The orange tablets had m. p. 98-99°. The yield was 4.7 g (43%).

Found %: N 25.55, 25.70. $C_{12}H_{14}N_4$. Calculated %: N 26.16.

Reaction of 2-methylquinolyl-6-dimethyltriazene with benzene. 2-Methylquinolyl-6-dimethyltriazene (4.2 g) was dissolved in 100 ml of dry benzene and 15 ml of glacial acetic acid (b. p. 118°). The mixture was boiled for 14 hours. The benzene solution was washed three times with water, the benzene removed, and the residue dissolved in chloroform and chromatographed on aluminum oxide. Benzene was used for elution. The triazene yield was 2.5 g. The m. p. was 98-99° (from ligroine).

5-Styrylquinaldine (I). 5-Aminoquinaldine (15.8 g) was dissolved in 25 ml of hydrochloric acid (d 1.19) and 20 ml of water. The solution was cooled to -10° and diazotized with 7.4 g of sodium nitrite in 12 ml of water. The diazonium chloride obtained was added to a cooled mixture of 14.8 g of cinnamic acid, 150 ml of acetone, 27.2 g of sodium acetate, and 5.2 g of cupric chloride in 12 ml of water. Vigorous evolution of gaseous products began. The carbon dioxide was absorbed in a saturated solution of barium hydroxide. Carbon dioxide liberation was complete at 35-40 minutes. The mixture was stirred at -2° for 2.5 hours and at room temperature for 4 hours. Acetone, chloroacetone, and quinaldine were steam distilled. The aqueous solution deposited 3.2 g of cinnamic acid. The residue in the flask was a dark mass which solidified on cooling. The black lumps removed from the distillation flask, ground up, washed with water on a filter, dried, dissolved in chloroform, filtered, and chromatographed on aluminum oxide. In a second chromatographic purification, benzene was used as eluant. The weight of base was 5.6 g. Recrystallization from methanol yielded 3.2 g (13%) of product. The light yellow tablets had m. p. 96-97°.

Found %: N 5.62; 5.56. $C_{18}H_{15}N$. Calculated %: N 5.71.

6-Styrylquinaldine (III). 6-Aminoquinaldine (15.8 g) was diazotized as described above. The diazonium chloride obtained was reacted with 14.8 g of cinnamic acid at -2° under conditions analogous to those in the synthesis of 5-styrylquinaldine. The acetone, chloroacetone and quinaldine were steam distilled from the reaction mixture. The residue was dried, dissolved in chloroform, and chromatographed twice on aluminum oxide. The yield of base was 6 g. Recrystallization from alcohol yielded 3.5 g of product. The colorless crystals had m. p. 156-157°.

Found %: N 5.64, 5.56. $C_{18}H_{15}N$. Calculated %: N 5.71.

The picrate crystallized from alcohol as yellow plates with m. p. 205-206°.

Found %: N 11.71, 11.68. $C_{24}H_{18}N_4$. Calculated %: N 11.81.

5-(4'-Phenylbutadienyl-1')-quinaldine(II). A mixture of 15.8 g of 5-aminoquinaldine, 17.4 g (0.1 mole) of styrylacrylic acid, 180 ml of acetone, 27.2 g of sodium acetate, and 5.2 g of cupric chloride in 12 ml of water was cooled to -5 to -7°. To the mixture was added the diazonium chloride and the mass stirred for 3 hours at -2° and for 5 hours at room temperature. Carbon dioxide was evolved copiously. To the reaction mass was added 0.1 g of hydroquinone and the mixture steam distilled. The base was chromatographed twice on aluminum oxide, eluted with benzene, and recrystallized from methanol. The yield was 4.3 g (15%). The light yellow tablets had m. p. 129-130°.

Found %: N 5.20, 5.21. $C_{20}H_{17}N$. Calculated %: N 5.16.

6-(4'-Phenylbutadienyl-1')-quinaldine (IV). 6-Aminoquinaldine (9.8 g) was dissolved in 15 ml of hydrochloric acid (d 1.19) and 12 ml of water. The solution was cooled to -5° and diazotized with 4.3 g of sodium nitrite in 7 ml of water. After standing for 8 minutes, the diazonium chloride was added to a mixture of 11 g of styrylacrylic acid, 100 ml of acetone, 16 g of sodium acetate and 3 g of cupric chloride in 6 ml of water, which was first cooled to -5°. The synthesis was then completed as described above. A large amount of carbon dioxide was evolved. After the addition of 0.1 g of hydroquinone, the mixture was steam distilled. The base was eluted with a mixture of benzene and chloroform (1:1). After recrystallization from benzene, the product formed coarse, lustrous, light yellow prisms with m. p. 200-201°. The yield was 4 g (23%).

Found %: N 5.26, 5.23. $C_{20}H_{17}N$. Calculated %: N 5.16.

2-Methyl-8-chloroquinoline. 2-Methyl-8-aminoquinoline (15.8 g) was diazotized in the usual way. The diazonium chloride obtained was added to a mixture consisting of 14.8 g of cinnamic acid, 27.2 g of sodium acetate,

TABLE 4

Compound No.	Name of dye	Amount taken				Yield, %	Melting point	Found			Calculated	
		base (g)	ethyl p-toluenesulfonate (g)	second component (g)*	pyridine (III) or anhydrous alcohol (IV) (ml)			element	content (in %)	empirical formula	element	content, (in %)
V	1,1'-Diethyl-5,5'-distyryl-quinocarbocyanine p-toluenesulfonate	0.49	0.44	I-1	III-4	25	249-250°	N	4.29, 4.24	C ₄₈ H ₄₄ O ₃ N ₂ S	N	3.84
VI	1,1'-Diethyl-5,5'-di-(4"-phenylbutadienyl-1")-quinocarbocyanine p-toluenesulfonate	0.54	0.44	I-1	III-6	16.6	262-263	N	3.79, 3.91	C ₆₂ H ₄₈ O ₃ N ₂ S	N	3.58
VIII	1,1'-Diethyl-6,6'-distyrylquinocarbocyanine p-toluenesulfonate	0.24	0.22	I-0.45	III-3	12.5	308-310	N	4.03, 4.03	C ₄₈ H ₄₄ O ₃ N ₂ S	N	3.84
IX	1,1'-Diethyl-6,6'-di-(4"-phenylbutadienyl-1")-quinocarbocyanine p-toluenesulfonate	0.54	0.44	I-1	III-3	25	300-301 with decomposition	N	3.84, 3.89	C ₆₂ H ₄₈ O ₃ N ₂ S	N	3.58
X	3-Ethyl-5-(1'-ethyl-5'-styryl-dihydroquinolylidene-2'-ethylidene)-thiazolidine-2-one-4	0.49	0.44	II-0.61	IV-10	51	256-257	S	14.42, 14.60	C ₂₈ H ₂₄ ON ₂ S ₂	S	14.41
XI	3-Ethyl-5-[1'-ethyl-5'-(r"-phenylbutadienyl-1")-dihydroquinolylidene-2'-ethylidene]-thiazolidine-2-one-4	0.54	0.44	II-0.61	IV-10	42	277-278	S	13.67, 13.74	C ₃₂ H ₂₆ ON ₂ S ₂	S	13.62
XII	3-Ethyl-5-(1'-ethyl-6'-styryldihydroquinolylidene-2'-ethylidene)-thiazolidine-2-one-4	0.24	0.22	II-0.29	IV-7	24.5	288-289 with decomposition	N	6.44, 6.37	C ₄₆ H ₄₄ ON ₂ S ₂	N	6.30
XIII	3-Ethyl-5-[1'-ethyl-6'-(4"-phenylbutadienyl-1")-dihydroquinolylidene-2'-ethylidene]-thiazolidine-2-one-4	0.54	0.44	II-0.61	IV-10	37	255-256	S	13.72, 13.67	C ₄₈ H ₄₆ ON ₂ S ₂	S	13.62

* Orthoformic ester - I; 3-ethyl-5-(acetamidomethylene)-rhodanine - II.

5.2 g of cupric chloride in 10 ml of water, and 150 ml of acetone, cooled to -5° . The mixture was stirred at -2° for 2.5 hours and at 20° for 5 hours. Carbon dioxide was liberated slowly and in a small amount. The reaction mass was then treated and purified in the usual way. Benzene was used for elution. The base contained halogen. The yield was 5.8 g. Recrystallization from methanol yielded fine, colorless tablets with m. p. $57-58^{\circ}$.

Found %: Cl 7.82, 7.87, 7.75. $C_{10}H_8Cl$. Calculated %: Cl 7.90.

According to literature data the melting point of 2-methyl-8-chloroquinoline is 64° [7].

General procedure for preparing quinocarbocyanines and merocyanines.

For the synthesis of dyes, appropriate bases were heated with ethyl p-toluenesulfonate on a paraffin bath at $155-160^{\circ}$ for 3 hours. To the quaternary salt was added dry pyridine and orthoformic ester. The mixture was boiled for 25-30 minutes. The precipitated quinocarbocyanine was collected by filtration, dissolved in the minimal amount of boiling pyridine, and filtered, and to the hot pyridine solution was added warm methyl alcohol until crystallization began. The mixture was heated to boiling and left to crystallize. The precipitated dye was collected, washed with methanol and ether, and dried in vacuum at $105-110^{\circ}$. The quinocarbocyanine (VI) was dissolved in 100 ml of boiling pyridine, filtered, and left to crystallize.

For the preparation of merocyanines, the appropriate quaternary salt was dissolved in anhydrous alcohol and to the solution was added 3-ethyl-5-(acetanilidomethylene)-rhodanine and triethylamine (0.6 ml). The mixture was heated on a boiling water bath for 30-40 minutes. After cooling, the precipitate was collected and washed with methanol, water, and again with methanol. The merocyanines were then recrystallized in the same way as quinocarbocyanines. The quinocarbocyanines were fine green crystals. The merocyanines formed lustrous, dark green crystals. Table 4 gives the conditions for synthesizing quinocarbocyanines and merocyanines and also analysis results.

1,1'-Diethyl-6,6'-diphenylquinocarbocyanine bromide (VII). A mixture of 0.43 g of 6-phenylquinaldine and 0.31 g of diethyl sulfate was heated on a paraffin bath at $140-145^{\circ}$ for 5 hours. To the quaternary salt obtained was added 0.8 g of orthoformic ester and 6 ml of pyridine. The mixture was boiled for 35 minutes and poured into a hot aqueous solution of potassium bromide. The dye was collected and recrystallized from alcohol. The yield was 0.3 g (27%). The fine dark crystals had m. p. 266° .

Found %: Br 13.30, 13.55. $C_{37}H_{33}N_2Br$. Calculated %: Br 13.69.

SUMMARY

1. The Meerwein reaction was used to synthesize four derivatives of quinaldine with styryl and ω -phenylbutadienyl radicals in the quinoline nucleus. Quaternary salts were obtained from the substituted quinaldines and ethyl p-toluenesulfonate.
2. Condensation of the quaternary salts with orthoformic ester and 3-ethyl-5-(acetanilidomethylene)-rhodanine yielded quinocarbocyanines and merocyanines with styryl and phenylbutadienyl groupings in the quinoline nucleus.
3. It was shown that the introduction of unsaturated substituents into the quinoline nucleus of merocyanine or quinocarbocyanine led to a strong displacement of the absorption maximum into the longwave region of the spectrum.

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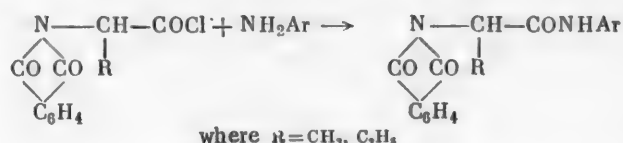
September 20, 1958

ARYLAMIDES OF ALIPHATIC D,L- α -AMINO ACIDS

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In connection with our other work we needed arylamides of aliphatic amino acids. D,L- α -Alanine and D,L- α -aminobutyric acid were used as starting materials. These acids were converted into phthalyl derivatives [1], which were then converted into N-phthalyl acid chlorides; the latter were reacted with aromatic amines.



The following compounds were obtained in this way: 1) N-Phthalyl-D,L- α -alanyl- β -aminonaphthalene, 2) N-phthalyl-D,L- α -alanyl-p-nitroaniline, 3) N-phthalyl-D,L- α -aminobutyryl-p-toluidine, 4) N-phthalyl-D,L- α -aminobutyryl-p-nitroaniline, and 5) N-phthalyl-D,L- α -alanyl-p-nitroaniline.

Catalytic reduction of the nitro groups in compounds 2 and 4 yielded N-phthalyl- α -alanyl-p-phenylenediamine and N-phthalyl- α -aminobutyryl-N-phenylenediamine. The phthalyl group was removed from these compounds by means of hydrazine hydrate [2]. The arylamides of α -alanine and α -aminobutyric acid thus formed were isolated as their hydrochlorides.

Attempts to synthesize arylamides of β -amino acids by the same methods did not give positive results. As starting materials we used β -alanine (D,L- β -aminopropionic acid) and p-nitroaniline. N-Phthalyl-D,L- β -aminopropionyl chloride was obtained by the method of Lederer and Pudles [3] and it condensed with p-nitroaniline without difficulty, but we were unable to remove the phthalyl group though the reaction was carried out by various methods and under different conditions. As reagents we used hydrazine hydrate or hydrazine sulfate in alcohol, 25% hydrochloric acid, and finally, hydrazine hydrate in glycerol. In all cases except for the latter, the starting materials were recovered. As a result of the action of hydrazine hydrate in glycerol, together with the starting material we isolated small amounts of p-nitroaniline, β -alanine, and phthalyl hydrazide.

We were also unable to reduce the nitro group in N-phthalyl-D,L- β -alanyl-p-nitroaniline. Various methods, including catalytic and noncatalytic ones, were used for the reduction experiments. This failure may be explained by the low solubility of N-phthalyl-D,L- β -alanyl-p-nitroaniline in almost all organic solvents.

EXPERIMENTAL

Starting materials. a) N-Phthalyl-D,L- α -alanine was obtained by the method of Billman and Harting [1] with the difference that equimolecular amounts of alanine and phthalic anhydride were heated for 40-45 minutes (instead of 15 minutes) at 160-165° (instead of 180-185°). The yield was 94%. The m. p. was 163-164°.

b) The acid chloride of N-phthalyl-D,L- α -alanine was obtained by heating N-phthalyl- α -alanine with an equal weight of phosphorous pentachloride, removing the phosphorous oxychloride in vacuum, and recrystallizing the residual material from ligroine. The yield was 83%. The m. p. was 69-70°.

Hydrochlorides of Arylamides of D,L- α -Amino Acids
$$\begin{array}{c} \text{R}-\text{CH}-\text{CO}-\text{NH}-\text{Ar} \cdot \text{HCl}, \\ | \\ \text{NH}_2 \end{array}$$
 where R = CH₃, C₂H₅

No	Acid radical	Ar	Amount taken				Recrystallization solvent
			starting N-phthalyl compound (in g)	85% aqueous solution of hydrazine hydrate (ml)	solvent (in ml)	2n hydrochloric acid (in ml)	
1	$\text{CH}_3-\text{CH}-\text{CO}-$ $ $ NH_2	$-\text{NHC}_6\text{H}_4\text{NO}_2$	2	0.4	1000 *	50	CH ₃ OH
2		$-\text{NHC}_6\text{H}_4\text{NH}_2$	2	0.5	CH_3OH 4.5 $\text{C}_2\text{H}_5\text{OH}$		$\text{C}_2\text{H}_5\text{OH}$ precip. by $\text{CH}_3\text{COOC}_2\text{H}_5$
3		$\beta\text{-C}_{10}\text{H}_7\text{NH}-$	5.6	1	300 $\text{C}_2\text{H}_5\text{OH}$ 4(h)	70	$\text{C}_2\text{H}_5\text{OH}$
4	$\text{CH}_3-\text{CH}_2-\text{CH}-\text{CO}-$ $ $ NH_2	$-\text{NHC}_6\text{H}_4\text{NO}_2$	2.73	0.5	$\text{C}_2\text{H}_5\text{OH}$ 4)		$\text{C}_2\text{H}_5\text{OH}$
5		$-\text{NHC}_6\text{H}_4\text{NH}_2$	1.42	0.22	$\text{C}_2\text{H}_5\text{OH}$ 4)	35	$\text{C}_2\text{H}_5\text{OH}$ precip. by $(\text{C}_2\text{H}_5)_2\text{O}$
6		$p\text{-CH}_3\text{C}_6\text{H}_4\text{NH}-$	0.16	0.03	10 $\text{C}_2\text{H}_5\text{OH}$	3.5	$\text{C}_2\text{H}_5\text{OH}$ precip. by $(\text{C}_2\text{H}_5)_2\text{O}$

* The use of such a large amount of solvent was due to the low solubility of N-phthalyl-D,L- α -alanyl-p-nitroaniline.

c) N-Phthalyl-D,L- α -aminobutyric acid was also obtained by the method in [1]. An increase in the heating time of α -aminobutyric acid with phthalic anhydride to 40-45 minutes (instead of 15 minutes) at a lower temperature (170-172° instead of 180-185°) led to an increase in yield from 65-84%. The m. p. was 95-96°.

d) The acid chloride of N-phthalyl-D,L- α -aminobutyric acid [4] was obtained by heating the phthalyl derivative with thionyl chloride. The excess thionyl chloride was removed in vacuum and traces of thionyl chloride were removed by the addition and subsequent distillation of chloroform. The acid chloride obtained (75%) yield was used for subsequent reactions without further purification.

1. N-Phthalyl-D,L- α -alanyl- β -naphthylamine. Over a period of 30 minutes, a solution of 16.2 g of β -naphthylamine in 40 ml of anhydrous ether was added to a solution of 13.45 g of the acid chloride of N-phthalyl- α -alanine in 60 ml of anhydrous ether at room temperature. The mixture was stirred at room temperature for 6 hours and then the separated material was collected and washed with ether and alcohol. The yield was 17.02 g (87.9%). For analysis, the substance was recrystallized twice from a large volume of alcohol. The m. p. was 164-165°. The colorless scales were soluble in alcohol, but insoluble in most organic solvents and water.

Found %: C 73.14; H 4.74; N 8.27. $\text{C}_{21}\text{H}_{16}\text{O}_3\text{N}_2$. Calculated %: C 73.24; H 4.65; N 8.13.

Evaporation of the mother solutions remaining after separation of the N-phthalyl- α -alanyl- β -naphthylamine yielded a mixture of substance which was recrystallized from alcohol and ethyl acetate to give 0.6 g of N-phthalyl- α -alanine (m. p. 163-164°) and 9.6 g of β -naphthylamine hydrochloride. The base with m. p. 110-111° was obtained from the latter.

2. N-Phthalyl-D,L- α -alanyl-p-nitroaniline. For the reaction we used 15 g of the acid chloride of N-phthalyl-D,L- α -alanine in anhydrous ether (380 ml) and 8.7 g of p-nitroaniline, also in anhydrous ether (600 ml). The yield was 19.34 g (90%). The substance was recrystallized twice from ethyl acetate. The m.p. was 252-253°. The long, colorless needles were insoluble in water and difficultly soluble in alcohol and ethyl acetate.

Melting point of crude substance	Yield (in %)	Melting point of re-crystallized substance	Found (%)				Calc. (%)			
			C	H	N	Cl	C	H	N	Cl
236—240°	91.3	245—247°	44.38	4.97	16.84	14.19	43.99	4.92	17.10	14.43
265—267	89.3	267—269	42.80	6.10	16.53		42.86	5.99	16.66	
243—244	88.5	244—245	62.28	6.07	11.25	14.18	62.27	6.03	11.17	14.14
237—238	87	244—245	45.95	5.83	16.15	13.33	46.24	5.43	16.18	13.65
273—275	88	276—277	45.00	6.67	16.19	26.65	45.11	6.44	15.79	26.64
166—168	81.8	169—170	57.85	7.61	12.51		57.76	7.49	12.24	

Found %: C 60.50; H 3.95; N 12.29. $C_{17}H_{15}O_3N_3$. Calculated %: C 60.17; H 3.86; N 12.38.

3. N-Phthalyl-D,L- α -aminobutyryl-p-nitroaniline. We used 6 g of N-phthalyl-D,L- α -aminobutyryl chloride in 20 ml of ethyl acetate and 4.06 g of p-nitroaniline. The reaction was carried out and the product isolated as in the previous experiments. We obtained 7.3 g (86.9 %) of product. It was recrystallized from ethyl acetate. The m. p. was 219–220°. We obtained colorless needles which were soluble in acetone and hot ethyl acetate, but insoluble in water.

Found %: C 61.05; H 4.05; N 11.75. $C_{18}H_{15}O_5N_3$. Calculated %: C 61.18; H 4.28; N 11.89.

4. N-Phthalyl-D,L- α -aminobutyryl-p-toluidine. We used 6 g of N-phthalyl-D,L- α -aminobutyryl chloride in 150 ml of a mixture of ether and ethyl acetate (1:1) and 3.15 g of p-toluidine in 40 ml of ethyl acetate. We obtained 5.04 g of product. Removal of the solvents from the filtrates and recrystallization of the residues from alcohol yielded a further 1.1 g of substance and a small amount of starting materials. The substance obtained was recrystallized twice from alcohol. The m. p. was 146–147°. The colorless needles were soluble in ethyl acetate, benzene, alcohol, and acetone and insoluble in water.

Found %: C 70.91; H 5.43; N 9.08. $C_{19}H_{18}O_3N_2$. Calculated %: C 70.78; H 5.62; N 8.69.

5. N-Phthalyl-D,L- α -alanyl-p-phenylenediamine. A suspension of 4.35 g of N-phthalyl-D,L- α -alanyl-p-nitroaniline, 4.0 g of Raney nickel catalyst, and 0.5 liter of anhydrous methyl alcohol was shaken in a hydrogen atmosphere at atmospheric pressure with gentle heating. The theoretical amount of hydrogen (880 ml) was absorbed in 3 hours. Removal of the catalyst and evaporation of the solvent left an oily substance which was triturated with a mixture of ether and alcohol. We obtained 3.85 g (97.2%) of a solid substance. A sample for analysis was recrystallized twice from alcohol. The m. p. was 163–164°. The amorphous yellow substance was soluble in alcohol and ethyl acetate and insoluble in water.

Found %: C 65.95; H 4.92; N 13.13. $C_{17}H_{15}O_3N_3$. Calculated %: C 66.00; H 4.88; N 13.58.

6. N-Phthalyl-D,L- α -aminobutyryl-p-phenylenediamine was obtained in exactly the same way as the previous compound.

We used 5.35 g of N-phthalyl-D,L- α -aminobutyryl-p-nitroaniline, 600 ml of alcohol, and 4 g of nickel catalyst. A volume of 1050 ml of hydrogen was absorbed. We obtained 4.25 g of product. The m. p. was 156-157°. The colorless crystals were soluble in alcohol and acetone and insoluble in water.

Found %: C 66.53; H 5.45; N 12.58. $C_{18}H_{17}O_3N_3$. Calculated %: C 66.85; H 5.30; N 12.93.

7. N-Phthalyl-D,L- β -alanyl-p-nitroaniline. We used 1.8 g of the acid chloride of N-phthalyl-D,L- β -alanine in 70 ml of anhydrous benzene and 1 g of p-nitroaniline, also in anhydrous benzene. The mixture was heated for 2 hours. The substance which precipitated on cooling was collected and washed with ethyl acetate and ether. We obtained 1.85 g of substance. The m. p. was 312-313° (decomp., from nitrobenzene). The yellow substance was insoluble in most organic solvents and difficultly soluble in nitrobenzene.

Found %: C 59.87; H 4.08; N 11.93. $C_{17}H_{15}O_3N_3$. Calculated %: C 60.17; H 3.86; N 12.38.

8. D,L- α -Alanyl-p-nitroaniline hydrochloride. To a solution of 2 g of N-phthalyl-D,L- α -alanyl-p-nitroaniline in 1 liter of methyl alcohol was added 0.4 ml of an 85% aqueous solution of hydrazine hydrate, the mixture boiled for 2 hours, and the solvent evaporated. The residual substance was treated with 50 ml of 2 N hydrochloric acid for 5 minutes at 40°. The phthalyl hydrazide was removed by filtration and the filtrate distilled in vacuum at 50-60° to leave 1.31 g (91.3%) of hydrochloride.

The substance was recrystallized twice from methyl alcohol for analysis. The m. p. was 245-247° (decomp.) with the apparatus preliminarily heated to 220° and a heating rate of 3° per minute. The colorless crystals were soluble in alcohol and water.

Found %: C 44.48; H 4.97; N 16.84; Cl 14.19. $C_9H_{11}O_3N_3 \cdot HCl$. Calculated %: C 44.00; H 4.92; N 17.10; Cl 14.43.

The remaining arylamides of D,L- α -alanine and D,L- α -aminobutyric acid in the form of the hydrochlorides were prepared from the corresponding N-phthalyl derivatives in exactly the same way. The compounds obtained and brief data on their synthesis and properties are given in the table.

SUMMARY

1. The reaction of the acid chlorides of N-phthalyl-D,L- α -alanine and N-phthalyl-D,L- α -aminobutyric acid with aromatic amines was studied and as a result of it we obtained arylamides of N-phthalyl-D,L- α -alanine and N-phthalyl-D,L- α -aminobutyric acid.

2. Arylamides of D,L- α -alanine and D,L- α -aminobutyric acid were synthesized by removal of the phthalyl group with hydrazine hydrate from the corresponding phthalyl derivatives.

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RADIOCHROMATOGRAPHIC STUDY OF THE FORMATION OF BUTYLENES IN THE SYNTHESIS OF BUTADIENE BY LEBEDEV'S METHOD

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During the synthesis of butadiene from ethyl alcohol by S. V. Lebedev's method there is gradual blocking of the catalyst surface by coke and this is accompanied by a change in the amount of products formed. It was established [1-3] that on a catalyst that has operated for a long period the amount of butylenes (α - and β -butylenes) increases and the amount of butadiene decreases. Until now the mechanism of butylene formation during the catalytic synthesis of butadiene has remained unexplained. It was considered [2 and 3] that butylenes mainly arose as a result of dehydration of butyl alcohol, formed during the synthesis of butadiene in an amount equivalent to 2-4% of the ethyl alcohol decomposed. However, when the synthesis is carried out on a coke-covered catalyst the amount of butylenes may reach 28-30% of the alcohol decomposed [1] and this cannot be explained by the dehydration of butyl alcohol alone. In this connection, the hypothesis was put forward that butylenes may be formed by hydrogenation of butadiene on a coke-covered catalyst [1].

TABLE 1

Synthesis of Butadiene on Lebedev Catalyst at 390°

Catalyst	Contact time τ (sec)	Composition of synthesis gas (in vol. %)				
		butadiene	butylenes			total
			α -C ₄ H ₈	β -C ₄ H ₈		
				trans	cis	
Fresh catalyst	15.7	30.4	2.5	1.8	3.0	7.3
Catalyst after synthesis containing 3% coke	15.5	9.4	10.0	13.0	10.0	33.0

Since the formation of butylenes occurs simultaneously with a large number of parallel reactions, to elucidate the mechanism of the process it seemed advantageous to use tracers in conjunction with radiochromatographic analysis [4]. The essence of the method consists of simultaneously plotting a normal chromatogram, giving the composition of the mixture, and a radiochromatogram, which makes it possible to calculate the specific molar radioactivity of the components.

For the work we used C¹⁴-labeled butadiene and α - and β -butylenes, which were synthesized together from labeled ethyl alcohol and then separated and isolated [4]. Standard Lebedev catalyst was used in the work. Table 1 gives the results of synthesis on two catalyst samples.

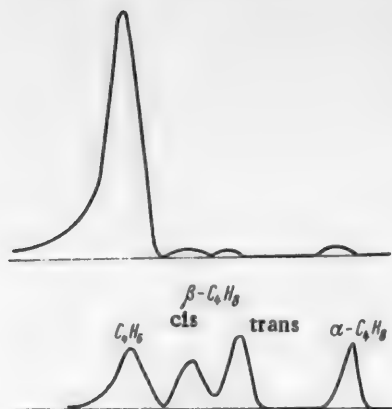


Fig. 1. Chromatogram of gas mixture from the synthesis of butadiene (C_4 fraction). Upper—coke-free catalyst; lower—coke-covered catalyst.

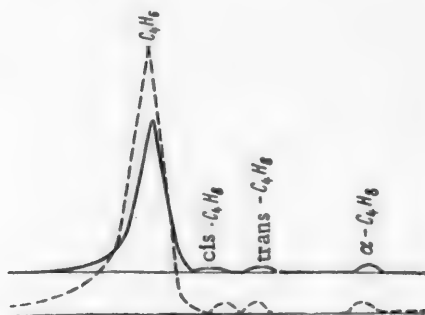


Fig. 2. Radiochromatogram of gas mixture from the synthesis of butadiene (C_4 fraction) from labeled ethyl alcohol on coke-free catalyst. Upper—concentration curve; lower—activity curve.

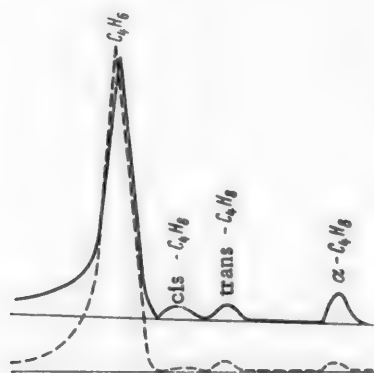


Fig. 3. Radiochromatogram of gas mixture from the synthesis of butadiene (C_4 fraction) from labeled ethyl alcohol (90%) with added n-butyl alcohol (10%) on coke-free catalyst. Upper—concentration curve; lower—activity curve.

The data obtained clearly show that when the synthesis was carried out on a coke-covered catalyst there was a sharp decrease in the butadiene content and an increase in the pseudobutylene content. This is also illustrated by chromatograms (Fig. 1). Special experiments showed that the dehydration of n-butyl alcohol on Lebedev catalyst at 390° yielded a mixture of α - and β -butylenes. In the next experiments butadiene synthesis was carried out on coke-free and coke-covered catalysts from a mixture of labeled ethyl alcohol (90%) and unlabeled n-butyl alcohol (10%). The amount of the latter was known to be greater than amounts formed during the synthesis of butadiene. For comparison, a synthesis from ethyl alcohol without additives was carried out each time in parallel. The gaseous synthesis products were analyzed radiochromatographically (Table and Figs. 2-4).

The molar activity of butadiene was taken as unity. The butylenes and butadiene obtained in the synthesis process should have had the same molar activity since both carbon atoms of the alcohol were labeled with C^{14} . The small difference between the molar activities of butadiene and butylenes was caused by experimental error. On comparing the results of butadiene synthesis from pure ethyl alcohol with the results of synthesis from a mixture of ethyl and butyl alcohols on coke-free catalyst, it should be noted that there was an increase in the amount of butylenes (by approximately 33%) and a decrease in their over-all molar activity (by approximately 36%). This can evidently be explained by dilution of the labeled butylenes, formed from labeled ethyl alcohol, by butylenes, formed by dehydration of unlabeled n-butyl alcohol. In synthesis on a coke-covered catalyst, the addition of butyl alcohol had hardly any effect on either the amount or the molar activity of the butylenes obtained. In this case butylenes are apparently formed by a different mechanism, namely, hydrogenation of butadiene formed from C^{14} -labeled ethyl alcohol.

From the data obtained one may assume that the formation of butylenes during the catalytic synthesis occurs by two routes, i. e., by dehydration of butyl alcohol on a coke-free catalyst and mainly by hydrogenation of butadiene on a coke-covered catalyst.

To check this assumption we studied the conversion of butadiene on a coke-covered Lebedev catalyst with hydrogen absent from the gas phase. For this purpose, nitrogen was first blown through a coke-covered catalyst for 30 minutes at 490° to remove polymerization products and then a mixture of butadiene (26.0%) and nitrogen (74.0%) was passed at 390° and the composition of the resultant gas determined.

To determine whether the coke simply transferred hydrogen from the gas phase, an attempt was made to enrich the coke in hydrogen. For this purpose a second experiment was carried out on the same sample in which hydrogen was blown through the catalyst at 390° for 1 hour

TABLE 2

Synthesis of Butadiene at 390° from a Mixture of Labeled Ethyl and Unlabeled Butyl Alcohols

Composition of mixture	Composition of gas										
	butadiene		butylenes						butylenes (in %)	average molar activity of butylenes	
	vol. %	molar activity	α -C ₄ H ₆		β -C ₄ H ₆						
			%	molar activity	trans		cis				
					%	molar activity	%	molar activity			
Coke-free catalyst											
C ₂ ¹⁴ H ₅ OH	31.6	1	1.8	0.9	2.8	0.8	2.0	0.8	6.6	0.83	
C ₂ ¹⁴ H ₅ OH (90%)	29.1	1	3.6	0.5	2.7	0.6	3.6	0.5	9.9	0.53	
N-C ₄ H ₉ OH (10%)											
Coke-covered catalyst											
C ₂ ¹⁴ H ₅ OH	9.4	1	9.8	0.8	14.9	0.8	8.4	0.8	33.1	0.8	
C ₂ ¹⁴ H ₅ OH (90%)	10.6	1	10.5	0.7	13	0.8	9.7	0.8	33.2	0.77	
N-C ₄ H ₉ OH (10%)											

and then a mixture of butadiene and nitrogen of the same composition as in the first experiment was passed. To check the possibility of hydrogenation of butadiene by hydrogen of the gas phase on the same catalyst, a mixture of butadiene (30%) and hydrogen (70%) was passed. The results are given in Table 3.

TABLE 3

Conversion of Butadiene on Coke-Covered Catalyst at 390° Under Various Conditions

Expt. No.	Catalyst treatment	Composition of starting mixture (in vol. %)			Composition of gas obtained (in %)*	
		butadiene	nitrogen	hydrogen	butadiene	butylenes
1	Catalyst treated with N ₂ before experiment (490°, 30 min)	26.0	74.0	—	4.85	8.95
2	Catalyst from Experiment 1 treated with N ₂ (490°, 1 hr) and then H ₂ passed	26.0	74.0	—	5.0	6.4
3	Catalyst from Experiments 1 and 2 treated with N ₂ (490°, 1 hr)	30.0	—	70.0	5.46	6.4

* The remaining products of thermal conversion of butadiene are not given in the table.

The gas from Experiment 1 contained 8.95% of butylenes, while the butadiene content fell from 26.90 to 4.85%. Treatment of the catalyst with hydrogen had no effect and the amount of butylenes was not increased. The gas from Experiment 3 contained the same amounts of butadiene and butylenes as in the previous experiments. Thus, it is evident that hydrogenation of butadiene by hydrogen from the gas phase on the given catalyst does not occur. The main reaction leading to the formation of butylenes is disproportionation of hydrogen between coke and butadiene.

TABLE 4

Composition of C_4 Hydrocarbons Obtained by Hydrogenation of Butadiene and Isomerization of α -Butylene on a Coke-Covered Catalyst

Starting compound	Composition of gas		
	α -butylene	β -butylene	
		cis	trans
Butadiene	22.1	32.4	45.5
α -Butylene	45.5	21.7	32.9
	35.4	36.2	28.6

To confirm the role of coke as a hydrogen donor, we carried out a series of experiments with circulation of butadiene through the same sample of coke-covered catalyst. The products obtained were analyzed chromatographically. In all experiments the butadiene was hydrogenated to butylenes with the amount of the latter decreasing from experiment to experiment. Figure 5 shows the results of these experiments. The percent butylene

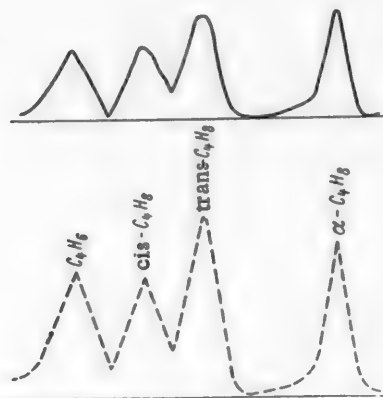


Fig. 4. Radiochromatogram of gas mixture from the synthesis of butadiene (C_4 fraction) from labeled ethyl alcohol (90%) with added *n*-butyl alcohol (10%) on coke-covered catalyst. Upper—concentration curve; lower—activity curve.

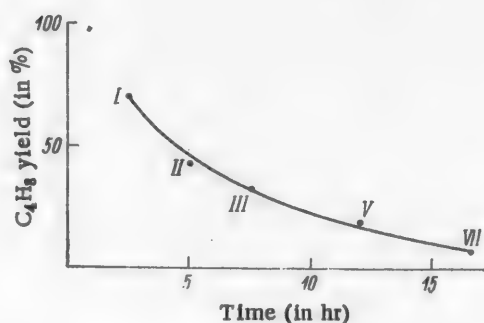


Fig. 5. Relation between the yield of butylenes from disproportionation of hydrogen between coke and butadiene and the operating time of the catalyst. The Roman figures denote the numbers of successive experiments.

content of the gas is plotted along the ordinate axis and the total time of operation of the catalyst, along the abscissa axis, while the Roman figures denote the numbers of successive experiments. The decrease in the amount of butylenes with an increase in the operating time of the coke-covered catalyst is evidently explained by impoverishment of the coke in hydrogen as the latter is consumed in hydrogenation of fresh portions of butadiene. This disproportionation of hydrogen between coke and butadiene yielded both α - and β -butylenes. Both could be products of direct addition of hydrogen with different types of conjugation of the bond system and also secondary isomerization products. Table 4 gives the composition of the gas obtained by hydrogenation of labeled butadiene and by isomerization of labeled α -butylene.

The data presented for butadiene show satisfactory agreement with the data presented by A. V. Frost [5] on the equilibrium of butylene isomerization at 400° (α -butylene 25%, β -butylene: cis 30%, trans 45%), while

the data from experiments with α -butylene show that isomerization of α -butylene also occurs on a coke-covered catalyst.

SUMMARY

1. The formation of butylenes during catalytic synthesis by S. V. Lebedev's method may occur as a result of two processes, namely, dehydration of butyl alcohol formed during synthesis on a coke-free catalyst, and disproportionation of hydrogen between coke and butadiene on a coke-covered catalyst. As the amount of coke on the catalyst increases, the second process becomes predominant.

2. During the synthesis of butadiene there is partial isomerization of α -butylene into cis- and trans- β -butylenes.

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PROPERTIES OF TRIHALOMETHYLSULFENYL CHLORIDES

K. A. Petrov and A. A. Neimysheva

Trichloromethylsulfenyl chloride, which was prepared in 1873 [1], remained the only representative of aliphatic sulfenyl chlorides for a long time. The chemical properties of this compound have been studied well by now and there is a voluminous literature on this problem. The most characteristic and important property of sulfenyl chlorides is their capacity to add to olefins at the multiple bond [2] and this is used in the synthesis of β -halogenated sulfides, which have high physiological activity.

The present work was devoted to studying the reaction of trichloromethyl- and fluorodichloromethylsulfenyl chlorides with substances containing a multiple bond. In contrast to other sulfenyl chlorides, trichloromethyl- and fluorodichloromethylsulfenyl chlorides react with olefins with difficulty to form β -halogenated sulfides containing a trihalomethyl group. Thus, trichloromethylsulfenyl chloride reacted with cyclohexene only on prolonged heating at 120°, while methylsulfenyl chloride added vigorously, even with cooling. Trihalomethylsulfenyl chlorides reacted even less readily with allyl chloride and added to propylene only at 100-110° under a pressure of about 100 atm. Trihalomethylsulfenyl chlorides could not be added to ethylene with heating under pressure, in the presence of benzoyl peroxide, or under ultraviolet irradiation. In the last two cases part of the sulfenyl chloride and a considerable amount of hexachlorodimethyl disulfide were recovered from the reaction.

Fluorodichloromethylsulfenyl chloride was obtained by two methods, namely, by replacement of chloride by fluorine in trichloromethylsulfenyl chloride with the aid of hydrogen fluoride and by cleavage of fluorodichloromethylsulfendiethylamide with hydrogen chloride.

EXPERIMENTAL

Trichloromethyl- β -chlorocyclohexyl sulfide. A mixture of 21.8 g of trichloromethylsulfenyl chloride and 10 g of cyclohexene was heated in a sealed tube at a bath temperature of 100° for 5 hours and then at 120° for 6 hours. Two vacuum distillations yielded 20 g (64%) of product.

B. p. 115° (3 mm), d_4^{24} 1.4058, n_D^{20} 1.5523.

Found %: S 12.11; Cl 53.49. $C_7H_{10}SCl_4$. Calculated %: S 11.94; Cl 52.98.

Trichloromethyl β,γ -dichloropropyl sulfide. A mixture of 17.8 g of trichloromethylsulfenyl chloride and 8.7 g of allyl chloride was heated in a sealed tube for 20 hours at 135-140°. After the tube had been opened, the liquid was vacuum distilled. The following fractions were isolated: 1st with b. p. 66° (50 mm) and 2nd with b. p. 115-116 (10 mm). Redistillation of the second fraction yielded 14.5 g (58 %) of product.

B. p. 109-110° (7.5 mm), d_4^{20} 1.6101, $n_D^{22.5}$ 1.5595.

Found %: S 12.55; Cl 67.36. $C_4H_5SCl_5$. Calculated %: S 12.19; Cl 67.56.

Trichloromethyl β -chloropropyl sulfide. A mixture of 7.1 g of trichloromethylsulfenyl chloride and 5 g (8.3 ml) of liquid propylene was placed in a 50-ml steel bomb with an internal glass tube, cooled in liquid nitrogen. The bomb was heated in an autoclave for 20 hours at 90-110° (the sulfide yield fell sharply with a decrease in heating time). After the heating, the bomb was again cooled in liquid nitrogen and opened. The bomb contents were vacuum distilled. Two distillations yielded 5 g (57%) of product.

B. p. 91-92° (11 mm), d_4^{20} 1.4267, n_D^{20} 1.5230.

Found %: S 12.92; Cl 59.85. $C_4H_6SCl_4$. Calculated %: S 13.44; Cl 59.57.

Fluorodichloromethylsulfenyl chloride. a) A stream of dry hydrogen chloride was passed for half an hour into a solution of 13 g of fluorodichloromethyl-N-diethylamide in 20 ml of absolute ether. The reaction proceeded with slight heat evolution. At the end of the reaction, the diethylamine hydrochloride was removed by filtration, washed several times with absolute ether, and dried. The ether was distilled from the filtrate and the residue distilled. Two distillations yielded 2.4 g (23%) of product. When the reaction was carried out with conc. HCl, the yield was low, evidently due to partial hydrolysis.

B. p. 52-53° (150 mm), 99.5-100.5°, d_4^{20} 1.6146, n_D^{20} 1.4828.

Found %: S 18.7; F 11.03; Cl 62.45. CSFCl_3 . Calculated %: S 18.88; F 11.21; Cl 62.83.

b) The reaction was carried out as above, but without solvent; after hydrogen chloride had been passed, without separation of the precipitate, the substance was vacuum distilled. After redistillation, the sulfenyl chloride boiled at 52-53° (150 mm). The yield was 55%.

c) A copper tube was charged with 30 g of trichloromethylsulfen-N-diethylamide and 30 g of anhydrous hydrogen fluoride. The mixture was left at room temperature for 4 days and then the excess hydrogen fluoride blown out and a small amount of dry potassium fluoride added to the reaction mass for complete removal of HF. The precipitate was removed by filtration and the filtrate consisted of two immiscible liquids. The lower layer was separated and distilled at atmospheric pressure. We isolated 6.4 g of product with b. p. 97-103°.

Found %: F 10.96. Calculated %: F 11.21.

d) Trichloromethylsulfenyl chloride (90 g) and 115 g of anhydrous hydrogen fluoride were reacted as described in Experiment "c". The liquid was decanted from the precipitate and vacuum distilled at 160 mm. The following fractions were collected: 1st with b. p. 55-65°, 18.7 g; 2nd with b. p. 65-95°, 17.3 g; 3rd with b. p. 97-98°, 28.5 g.

Redistillation of the first fraction yielded a substance with b. p. 98-102°. The yield was 23%. The third fraction was original trichloromethylsulfenyl chloride.

Fluorodichloromethyl β -Chlorocyclohexyl sulfide. A mixture of 2.5 g of fluorodichloromethylsulfenyl chloride and 3 g of cyclohexene was heated in a sealed tube at a bath temperature of 120° for 1.5 hours. After the tube had been opened, the reaction mixture was vacuum distilled. The yield was 3 g (80%).

B. p. 94-95° (2 mm) or 105-106° (5 mm), d_4^{19} 1.3630, n_D^{19} 1.5200.

Found %: S 12.3; F 6.9; Cl 42.15. $\text{C}_7\text{H}_{10}\text{SFCl}_3$. Calculated %: S 12.72; F 7.55; Cl 42.35.

Fluorodichloromethyl β,γ -dichloropropyl sulfide. A mixture of 20.45 g of fluorodichloromethylsulfenyl chloride and 10.9 g of allyl chloride was heated in a sealed tube for 15 hours at a bath temperature of 120°. After the tube had been opened, the contents were vacuum distilled. The yield was 21.7 g (73%).

B. p. 96° (8 mm) or 92.5-93.5° (7 mm), d_4^{20} 1.5198, n_D^{21} 1.5150.

Found %: S 12.84; F 7.58; Cl 57.13. $\text{C}_4\text{H}_5\text{SFCl}_4$. Calculated %: S 13.01; F 7.72; Cl 57.72.

Fluorodichloromethyl β -chloropropyl sulfide. The reaction of propylene with fluorodichloromethylsulfenyl chloride was carried out under the same conditions as with trichloromethylsulfenyl chloride with heating for 10 hours. The yield was 69%.

B. p. 102-103° (55 mm), d_4^{20} 1.3945, n_D^{24} 1.4915.

Found %: S 15.64; F 8.68; Cl 50.58. $\text{C}_4\text{H}_5\text{SFCl}_3$. Calculated %: S 15.13; F 8.98; Cl 50.35.

SUMMARY

1. A method was developed for preparing fluorodichloromethylsulfenyl chloride by the action of hydrogen fluoride on trichloromethylsulfenyl chloride and by decomposition of fluorodichloromethylsulfendiethylamide with hydrogen chloride.

2. The addition of trichloro- and fluorodichloromethylsulfenyl chlorides to cyclohexene, allyl chloride, and propylene was investigated and the corresponding sulfides prepared.

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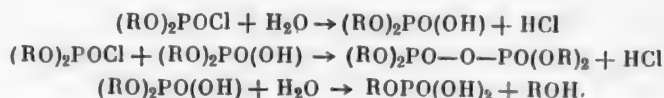
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DIALKYL PHOSPHATES AND PYROPHOSPHATES

K. A. Petrov, N. K. Bliznyuk, and F. L. Maklyaev

Dialkyl phosphates are monobasic acids, separate representatives of which exceed phosphoric acid in strength. Despite their ease of formation, these substances have been studied little up to the present time, which to a considerable extent is connected with the difficulty of isolating acid phosphates as they are generally undistillable or difficultly distillable* liquids.

Dialkyl phosphates and other impurities are formed in considerable amounts in the preparation of trialkyl phosphates and pyrophosphates and their hydrolysis. They are obtained very readily by hydrolysis of dialkyl chlorophosphates. In the latter case, monoalkyl phosphates, pyrophosphates, and phosphoric acid are formed as impurities.



It is impossible to isolate individual dialkyl phosphates from this complex mixture by fractional distillation. It was only possible to obtain dialkyl phosphates in a comparatively pure form by conversion of the phosphates to salts and then fractional crystallization [1]. At the present time the best method of preparing these substances is that of Toy [2], which is based on hydrolysis of pyrophosphates under definite conditions. Pure dimethyl, diethyl, and dipropyl phosphates were prepared by this method [2, 3].

In the present investigation a simple method was developed for preparing and isolating water insoluble or difficultly soluble dialkyl phosphates without their conversion to salts. The method was based on hydrolysis of chlorophosphates with excess water under drastic conditions, excluding the formation of pyrophosphates; the hydrogen chloride, monoalkyl phosphates and other impurities formed in the reaction were separated from the main reaction product by repeated washing with water. Water dissolved in the dialkyl phosphates was removed in vacuum by means of benzene added to the phosphate. Crude dialkyl chlorophosphates, obtained by chlorination of dialkyl phosphites, could be used successfully for hydrolysis. Dialkylphosphoric acids with traces of mono- and trialkyl phosphates were obtained in up to 80% yield by the method examined.

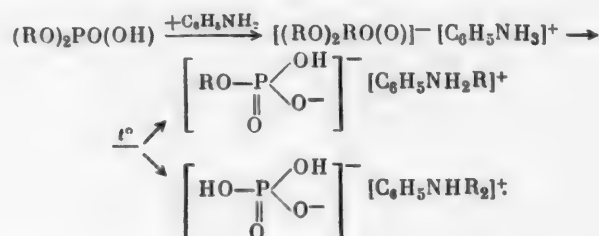
Dialkyl phosphates could also be obtained in satisfactory yield by reaction of phosphorus oxychloride with aqueous alcohol solutions, containing 1 mole of water to 2 moles of alcohol.



Since water reacts with phosphorus oxychloride more vigorously than alcohols, under certain conditions this reaction could lead to the formation of considerable amounts of phosphoric acid and mono- and trialkyl phosphates. In order to eliminate or reduce these side processes to a minimum, the reaction had to be carried out with simultaneous mixing of stoichiometric amounts of phosphorus oxychloride and aqueous alcohol solution at an elevated temperature so that the oxychloride reacted at a high rate not only with water, but also with alcohol. The dialkyl phosphates were isolated in the same way as when they were prepared by hydrolysis of chlorophosphates.

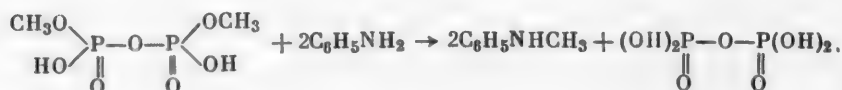
*Lower dialkyl phosphates were recently distilled successfully in high vacuum [2,3].

Up to the present the chemical properties of dialkylphosphoric acids have hardly been studied at all. In this work it was shown that like trialkyl phosphates [4] and chlorophosphates [5], dialkyl phosphates have the capacity to alkylate. At an elevated temperature they will alkylate aromatic amines, in particular, aniline; secondary and tertiary aliphatic-aromatic amines are thus obtained in satisfactory yields. When a dialkylphosphoric acid is mixed with a primary amine a salt is first formed and on heating, this is converted into salts of secondary or tertiary amines and monoalkylphosphoric or phosphoric acids.



The free bases were liberated by treatment of the salts with alkali. The amines were separated by fractional distillation and with the aid of benzenesulfonyl chloride.

Like dialkyl phosphates, dialkyl pyrophosphates also alkylate aromatic amines comparatively readily. Thus, heating a mixture of dimethyl pyrophosphate with aniline in a molar ratio of 1 : 2 formed largely N-methylaniline.



Dimethylaniline was obtained when excess pyrophosphate was used and when the reaction was carried out under more drastic conditions. Since dialkyl pyrophosphates are obtained by simply mixing stoichiometric amounts of alcohol and phosphorus pentoxide [6], in some cases alkylation with acid pyrophosphates may be of practical interest.

Formula	d_4^{20}	n_D^{20}	MR		Yield (in %)	Found		Calc.	
			found	calc.		P (%)	equivalent (by titration)	P (%)	equivalent (by titration)
(n-C ₄ H ₉ O) ₂ P(O)(OH)	1.0876	1.4337	50.35	51.01	79	14.68	208.5	14.75	210.2
(iso-C ₄ H ₉ O) ₂ P(O)(OH)	1.0840	1.4320	51.31	51.01	71	14.63	213.2	14.75	210.2
(n-C ₅ H ₁₁ O) ₂ P(O)(OH)	1.0660	1.4395	58.87	60.25	69	13.21	242.1	13.01	238.3
(iso-C ₅ H ₁₁ O) ₂ P(O)(OH)	1.0651	1.4375	58.69	60.25	64	12.95	240.4	13.01	238.3

EXPERIMENTAL

Dialkyl phosphates. a) Chlorine was slowly passed into 1 mole of dialkyl phosphite with cooling in ice and salt until there was a negative reaction for trivalent phosphorus (test with mercuric chloride). Then air was passed through the mixture for 2 hours to remove excess chlorine and the hydrogen chloride formed. With vigorous stirring, 100 ml of water was added to the crude dialkyl chlorophosphate obtained and the mixture was carefully heated to 100° and kept at this temperature for 20 minutes. When it had cooled, to the mixture was added 250 ml of benzene, the aqueous layer separated, and the organic layer washed repeatedly with water until chlorine ion was absent. The benzene solution was first kept at room temperature and then heated to constant weight. The residue was practically pure dialkyl phosphate. The properties, yields, and analysis data of the substances obtained are given in the table.

b) Into a flask fitted with a bubbler, thermometer, two graduated dropping funnels, and a reflux condenser was placed 100 ml of dry carbon tetrachloride. The solvent was heated to 50° and a rapid stream of dry air sucked through for stirring the mixture while 1 mole of phosphorus oxychloride and aqueous alcohol solution (from 2 moles of alcohol and 1 mole of water) were simultaneously added at such a rate that the temperature was kept at about 55°. After the reagents had been mixed, air was sucked through for a further hour. Then 250 ml of benzene was added and the reaction mixture treated as described above. The dialkyl phosphates synthesized by this method were identical with the products obtained by hydrolysis of chlorophosphates. The yield was 55-60%.

Alkylation of aniline with dibutyl phosphate. a) A mixture of 25.2 g of dibutyl phosphate and 18.6 g of aniline was heated until the temperature reached 225° (about 5 hours). To the cooled mixture was added 200 ml of 20% sodium hydroxide. The oily layer was separated and the aqueous layer extracted with ether. The ether solution was mixed with the oily layer, dried over solid alkali, and distilled. We isolated: 1) 2.5 g of alinine; 2) 16.0 g (53.5%) of N-butylaniline with b. p. 117-118° (10 mm), 232-235° (750 mm), d_4^{20} 0.9330, n_D^{20} 1.5330.

Found %: N 9.30. $C_{10}H_{15}N$. Calculated %: N 9.36.

3) 4 g (9.75%) of dibutylaniline with b. p. 140-142° (10 mm), 260-264° (750 mm), d_4^{20} 0.9157, n_D^{20} 1.5220.

Found %: N 6.67. $C_{14}H_{23}N$. Calculated %: N 6.82.

Literature data [8]: For N-butylaniline: b. p. 235° (720 mm); for dibutylaniline: b. p. 262.8°.

b) A mixture of 14 g of aniline and 37.8 g of dibutyl phosphate was heated in a sealed tube for 10 hours at 250°. After treatment as described above, distillation yielded a fraction (27 g) with b. p. 117-175° (10 mm), consisting of monobutyl- and dibutylaniline. For separating them, 300 ml of a 12% solution of potassium hydroxide was added, followed by 38.1 g of benzenesulfonyl chloride with stirring and the mixture heated until the smell of the acid chloride disappeared. The cooled mixture was extracted with ether and the extract treated with 50 ml of hydrochloric acid (1 : 1). After evaporation of the solvent, the residue was heated in vacuum to constant weight. We obtained 17 g (39%) of crude N-butyl-N-phenylbenzenesulfonamide as a thick, undistillable liquid.

Found %: N 4.55. $C_{16}H_{19}O_2NS$. Calculated %: N 4.85.

Treatment of the aqueous layer with concentrated alkali yielded 12 g (39%) of dibutylaniline with b. p. 260-265° (750 mm).

Alkylation of aniline with dimethyl pyrophosphate. Methyl alcohol (11.7 g) was added dropwise with stirring to 26 g of phosphorus pentoxide. To the pyrophosphate obtained was added 34 g of aniline and the mixture boiled for 2.5 hours (the temperature in the mixture at the end of the reaction was 194°). Treatment with alkali liberated an oil which was fractionated to yield 21 g (53.5%) of N-methylaniline.

B. p. 72-73° (10 mm), 190-192° (750 mm), d_4^{20} 0.9852, n_D^{20} 1.5710.

Literature data [8]: B. p. 195.5°, $d_4^{21.5}$ 0.986, $n_D^{21.5}$ 1.5702.

Found %: N 12.87. C_7H_9N . Calculated %: N 13.01.

For identification purposes the amine obtained was treated with nitrous acid to give an 85% yield of N-methyl-N-nitrosoaniline [7]; b. p. 132-122° (11 mm).

Literature data [7]: B. p. 135-137° (13 mm).

Found %: N 20.32. $C_7H_9ON_2$. Calculated %: N 20.55.

Alkylation of aniline with dibutyl pyrophosphate. Under conditions analogous to those in the alkylation with dimethyl pyrophosphate,* from 32.8 g of phosphorus pentoxide, 34.2 g of n-butyl alcohol, and 43 g of aniline we obtained 36 g (52%) of monobutylaniline with b. p. 117-118° (10 mm) and 7 g of dibutylaniline with b. p. 140-142° (10 mm). For identification, the monobutylaniline was converted into N-butyl-N-nitrosoaniline, which decomposed during a distillation attempt and was therefore analyzed in the crude state.

Found %: N 15.3. $C_{10}H_{14}ON_2$. Calculated %: N 15.7.

The crude nitroso compound was reduced with stannous chloride to the starting amine [7] in 72% yield.

*The boiling point of the reaction mixture had risen to 225° at the end of the reaction.

SUMMARY

1. A method was developed for preparing dialkyl phosphates of higher alcohols by hydrolysis of chlorophosphates and by reaction of phosphorus oxychloride with aqueous alcohol solutions.
2. It was shown that dialkyl phosphates and dialkyl pyrophosphates are capable of alkylating aromatic amines.

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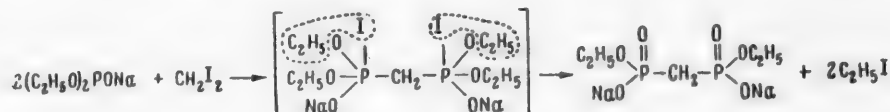
REACTION OF SODIUM DIALKYL PHOSPHITES WITH PHOSPHONATES

K. A. Petrov, N. K. Bliznyuk, M. A. Korshunov, F. L. Maklyaev,
and A. N. Voronkov

It is known [1] that the action of alkyl halides on salts of dialkylphosphorous acids forms dialkylphosphonates (Michaelis-Becker reaction):



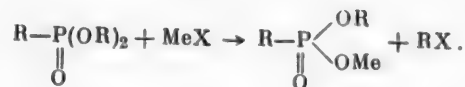
However, in some cases in the alkylation of sodium dialkylphosphites with alkyl halides, ester salts of alkylphosphinic acids are formed together with neutral esters [2]. Cases are also known where the Michaelis-Becker reaction forms only ester salts of alkylphosphinic acids. Thus, for example, by the action of methyl iodide or chloride on sodium diethylphosphite, P. Nylen [3] obtained the disodium salt of the diethyl ester of methylenediphosphonic acid instead of the expected neutral ester. To explain the formation of the ester salt of methylenediphosphonic acid the author assumed that in this case the sodium phosphonium halide decomposed with the elimination of ethyl iodide and not sodium iodide.



Other investigators also gave similar explanations for the anomalous course of the Michaelis-Becker reaction [2].

Leaving to one side the problem of the possibility of the formation of a salt-like addition product in the Michaelis-Becker reaction, it should be noted, nevertheless, that the explanation of the anomalous course of the reaction, leading to the formation of the ester salt, is incorrect. It is difficult to assume that a sodium phosphonium halide, even if it is formed in this reaction, decomposed with the elimination of sodium halide in some cases and of alkyl halide in others.

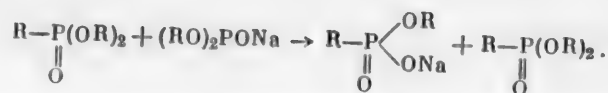
In our opinion, neutral esters of alkylphosphinic acids are first formed in all cases in the alkylation of sodium dialkylphosphites and the formation of ester salts is the result of secondary processes. These secondary processes are caused by the comparatively high alkylating capacity of neutral esters of alkylphosphinic acids. For example, it is known that these esters alkylate alkali-metal halides [4] to form alkyl halides and ester salts of alkylphosphinic acids.



This alkylation, however, proceeds only at high temperature (about 200°) and can hardly occur under the conditions of the Michaelis-Becker reaction.

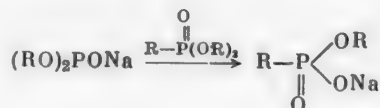
During the Michaelis-Becker reaction, the reaction mixture contains the neutral ester of the alkylphosphinic acid together with the alkyl halide. In view of this circumstance, there are no grounds for excluding the reaction

of this ester with the sodium dialkylphosphite. This reaction forms the salt of the alkylphosphinic ester and the dialkylphosphonate.



The alkylations of sodium phosphites by the alkyl halide, and the phosphonates formed are competing reactions. In individual cases when the alkylating capacity of the phosphonates is higher than that of the alkyl halides used, ester salts are formed predominantly rather than neutral esters.

It is not difficult to see that in the reaction examined the dialkylphosphonate would be regenerated and consequently small amounts of it would be sufficient for the conversion of large amounts of sodium phosphite into the corresponding ester salt of the alkylphosphinic acid. The arguments presented also served as the basis of the discovery of a new reaction for converting phosphites into phosphonates.



In this work it was shown that treatment of sodium dialkylphosphites with neutral esters of alkylphosphinic acids in small amounts (4-5% of the weight of phosphite) formed alkylphosphonates in almost quantitative yield. The latter were isolated in a discrete state and were also hydrolyzed to alkylphosphinic acids, which were then converted into aniline salts and the corresponding diacid chlorides. Instead of neutral esters of alkylphosphinic acids, it was possible to add small amounts of alkyl halides, which reacted with the sodium dialkylphosphite to form the neutral ester of the alkylphosphinic acid, required for converting the whole of the sodium phosphite into the ester salt of the alkylphosphinic acid.

The reaction was studied on the examples of the alkylation of sodium salts of dimethyl-, diethyl-, and dibutylphosphorous acids. The corresponding alkylating agents used were dimethyl methylphosphinate, diethyl ethylphosphinate, and dibutyl butylphosphinate. The reaction was carried out in alcohols and also in toluene.

It should be noted that sodium dialkylphosphites were obtained not only by the action of metallic sodium on dialkyl phosphites, but also by neutralization of the phosphite with the calculated amount of concentrated alkali. The latter method is of practical value and makes this reaction more suitable for preparative synthesis of alkylphosphinic acids and their derivatives than the Michaelis-Becker reaction. With the Michaelis-Becker reaction, only sodium phosphites obtained by the action of metallic sodium on acid phosphites in anhydrous solvents are alkylated. The latter circumstance reduces the value of this reaction and makes it inconvenient for the preparation of alkylphosphonates on an industrial scale.

Our discovery of the conversion of salts of dialkyl phosphites into phosphonates is of practical interest and makes it possible to explain the formation of side products in the Michaelis-Becker reaction.

EXPERIMENTAL

Sodium salt of methyl methylphosphinate. To 0.1 mole of the alcohol solution of alcoholate, obtained from 2.3 g of sodium and 30 ml of anhydrous methyl alcohol, was added 11 g (0.1 mole) of dimethyl phosphite dropwise. To the solution of sodium dimethylphosphite obtained was added 0.6 g of dimethyl methylphosphinate. The reaction mixture was heated for 7 hours in a sealed tube on a boiling water bath.* The end of the reaction was determined by the absence of trivalent phosphorus. ** Removal of the solvent and heating in vacuum yielded

* Completion of the reaction at the boiling point of methyl alcohol required 22-25 hours.

** A sample of 2-3 drops of solution was diluted to 1 ml with water, acidified with hydrochloric acid, and treated with mercuric chloride solution. The mixture was heated to boiling and then cooled. A precipitate of mercurous chloride was formed when trivalent phosphorus was present.

13 g (98.5%) of salt, which was purified by solution in methyl alcohol and subsequent precipitation with ether. The white hygroscopic powder had m. p. 435-440°.

Found %: P 23.75, 23.60; OCH_3 23.28. $\text{C}_2\text{H}_5\text{O}_3\text{PNa}$. Calculated %: P 23.49; OCH_3 23.49.

For identification, the ester salt was converted into methylphosphinic acid and the latter into its aniline salt.

A mixture of 6.6 g of the sodium salt of methyl methylphosphinate and 30 ml of concentrated hydrochloric acid was heated on a boiling water bath for 4 hours. After the hydrolysis, the solution was evaporated to dryness in vacuum on a water bath and the residue treated with propyl alcohol. The alcohol solution was evaporated to dryness; the dry residue [4.3 g (90%)] was methylphosphinic acid: M. p. 101-104° (from benzene). Literature data [3]: M. p. 104°. A mixed melting point with methylphosphinic acid obtained by hydrolysis of dimethyl methylphosphonate was not depressed.

To a solution of 4 g of methylphosphinic acid in 30 ml of n-propyl alcohol was added the calculated amount of aniline. We isolated 6 g (76%) of the aniline salt of methylphosphinic acid with m. p. 149-150° (from propyl alcohol).

Found %: N 7.49. $\text{C}_7\text{H}_{12}\text{O}_3\text{NP}$. Calculated %: N 7.41.

The aniline salt of methylphosphinic acid, obtained by hydrolysis of dimethyl methylphosphonate, had the same melting point. A mixed melting point of the two salts was not depressed.

Sodium salt of ethyl ethylphosphinate. a) To 2.3 g of sodium (wire) in 40 ml of dry toluene was added 13.8 g of diethyl phosphite dropwise. After the sodium had dissolved, 0.7 g of diethyl ethylphosphinate was added and the mixture boiled under reflux until no trivalent phosphorus remained (about 7 hours), and then the solution was evaporated to dryness in vacuum with heating. We obtained 15.8 g (99%) of crude salt, which had m. p. 420-426° after purification as described above.

Found %: P 19.49; C 29.65; H 6.08. $\text{C}_4\text{H}_{10}\text{O}_3\text{PNa}$. Calculated %: P 19.38; C 30.00; H 6.29.

A mixed melting point with the ester salt obtained by neutralization of monoethyl ethylphosphinate was not depressed.

b) With cooling, 10 g of 40% aqueous sodium hydroxide solution was carefully added to 13.8 g of diethyl phosphite in a Wurtz flask. The solution was then evaporated to dryness in vacuum on a water bath. To the powdered residue were added 40 ml of toluene and 0.7 g of diethyl ethylphosphinate. The reaction was then carried out as in Experiment "a". We obtained 15.7 g (98%) of salt, which was identical with the ester salt described in Experiment "a".

A mixture of 8 g of the sodium salt of ethyl ethylphosphinate and 30 ml of concentrated hydrochloric acid was heated in a sealed tube for 4 hours at 120-130°. Ethylphosphinic acid was isolated in the same way as methylphosphinic acid. We obtained 5 g (91%) of crude ethylphosphinic acid, which was treated with the calculated amount of an alcohol solution of aniline. We isolated 7.7 g (75%) of aniline salt with m. p. 143-144° (from isopropyl alcohol).

Found %: N 6.80. $\text{C}_8\text{H}_{14}\text{O}_3\text{PN}$. Calculated %: N 6.89.

The aniline salt of ethylphosphinic acid, obtained by hydrolysis of diethyl ethylphosphonate, melted at the same temperature. A mixed melting point of the two salts was not depressed.

Diacid chloride of ethylphosphinic acid. To 16 g of the sodium salt of ethyl ethylphosphinate was added 41.7 g of phosphorous pentachloride in portions (strong evolution of heat and voluminous liberation of ethyl chloride). The mixture was heated in a sealed tube for 3 hours at 130-135° for completion of the reaction. The sodium chloride was separated by decantation. After evaporation of the phosphorous oxychloride, the residue was vacuum distilled. We obtained 8.8 g (60%) of product.

B. p. 71-72° (12 mm), d_4^{20} 1.3758, n_D^{20} 1.4645. According to data in [5]: B. p. 175°.

Found %: Cl 48.75. $\text{C}_2\text{H}_5\text{OPCl}_2$. Calculated %: Cl 48.30.

Sodium salt of butyl butylphosphinate. a) Under conditions analogous to those in the synthesis of the ester salt of ethylphosphinic acid, but at 150-160° (sealed tube), 0.1 mole of sodium dibutylphosphite (from 2.3 g of

sodium and 19.4 g of dibutyl phosphite) and 0.4 g of butyl bromide yielded 20.8 g (96.5%) of salt with m. p. 416-420° (from butyl alcohol).

Found %: P 14.56, 14.65. $C_8H_{18}O_3PNa$. Calculated %: P 14.35.

A mixed melting point with the salt obtained by neutralization of monobutyl butylphosphinate was not depressed.

b) Alkylation of 0.1 mole of sodium dibutylphosphite (from 19.4 g of dibutyl phosphite and 10 g of a 40% aqueous solution of sodium hydroxide) with 1 g of dibutyl butylphosphinate under analogous conditions yielded 20.5 g (95%) of ester salt, identical with that described in Experiment "a".

A mixture of 10.8 g of the sodium salt of butyl butylphosphinate and 30 ml of concentrated hydrochloric acid was heated in a sealed tube for 4 hours at 160-170°. The butylphosphinic acid was isolated in the same way as methylphosphinic acid. We obtained 6.5 g (94%) of butylphosphinic acid with m. p. 104-106° (from benzene). According to data in [6]: M. p. 103.5-104°. A mixed melting point with an authentic sample was not depressed.

Butylphosphinic acid (6 g) was treated with the calculated amount of an alcohol solution of aniline. We obtained 7.1 g (70%) of aniline salt with m. p. 126-128° (from butyl alcohol).

Found %: N 6.14. $C_{10}H_{18}O_3PN$. Calculated %: N 6.06.

The aniline salt of butylphosphinic acid, obtained by hydrolysis of dibutyl butylphosphinate, had the same melting point. A mixed melting point of the two salts was not depressed.

Diacid chloride of butylphosphinic acid. Under conditions analogous to those in the synthesis of the diacid chloride of ethylphosphinic acid, 10.8 g of the sodium salt of butyl butylphosphinate and 20.8 g of phosphorous pentachloride yielded 7.1 g (80%) of product.

B. p. 96-97° (15 mm), d_4^{20} 1.2415, n_D^{20} 1.4615.

Found %: Cl 40.86. $C_4H_9OPCl_2$. Calculated %: Cl 40.57.

SUMMARY

It was shown that under the action of small amounts of dialkylphosphonates or alkyl halides, sodium salts of dialkyl phosphites are converted into salts of alkylphosphinic esters.

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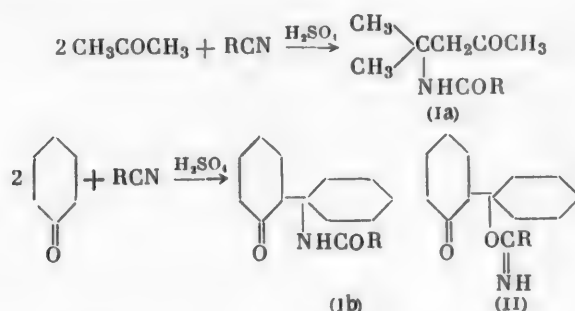
CONDENSATION OF KETONES WITH NITRILES UNDER THE CONDITIONS OF THE RITTER REACTION

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Moscow State University

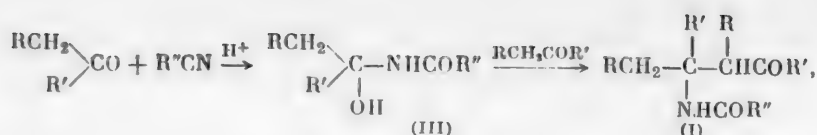
In connection with the synthesis of some physiologically active substances on the basis of the Ritter reaction [1], we observed that during the reaction of acetone and cyclohexanone with benzonitrile in the presence of concentrated sulfuric acid, crystalline compounds were formed in good yield. An analogous result was also obtained by the reaction of cyclohexanone with acetonitrile. Since we were unable to find any reliable information in the literature on the possibility of such a condensation, we investigated this reaction in more detail.

The compounds formed contained nitrogen and had weakly basic properties; they dissolved in concentrated acids and were liberated unchanged when the solution was treated with alkali. Hydrolysis of the condensation product of cyclohexanone and benzonitrile with 5% hydrochloric acid yielded cyclohexanone, which was identified as the semicarbazone, and benzoic acid. Analysis of the compounds obtained showed that they were formed by condensation of two molecules of ketone with a molecule of nitrile. The compound obtained by condensation of acetone with benzonitrile was found to be identical with 4-methyl-4-benzamidopentanone, described by Gabriel [2]. Thus, the substances we obtained were derivatives of β -acylamino ketones and the over-all result may be expressed by the equations:

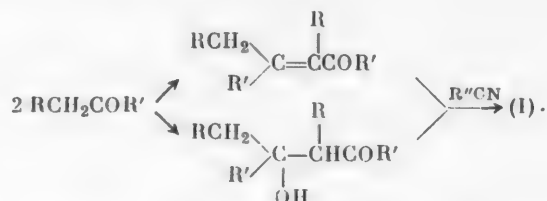


The structures (Ia) and (Ib) presented are in conformity with the properties of the compounds we obtained as the instability of N-tert-alkylamides toward acid hydrolysis [1] and the capacity of α,β -unsaturated ketones for hydrolytic cleavage of the carbon-carbon bond are well known. It is also known that the basic properties of groups attached to a tertiary carbon are noticeably increased; therefore, it is not surprising that the acylamino ketones obtained behaved as weak bases. Bruson et al. [3] described the condensation of cyclohexanone with benzonitrile in the presence of aluminum chloride, when they obtained a substance identical with that formed under our conditions but ascribed to this compound and its analogs, obtained from other nitriles, the structure of imino esters (II). Our data show that the compounds obtained actually corresponded to the structure of β -acylamino ketones (Ib).

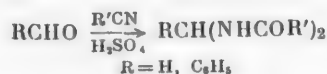
The condensation of ketones with nitriles, leading to the formation of β -acylamino ketones, may proceed according to one of two schemes. Either the initial condensation product, the hydroxymethylamide (III), then reacts with a second molecule of ketone by a type of acylaminomethylation reaction, giving the acylamino ketone (I):



or, on the other hand, under the action of sulfuric acid, the ketone first undergoes crotonic or aldolic condensation, the products of which then undergo a Ritter reaction with the nitrile:

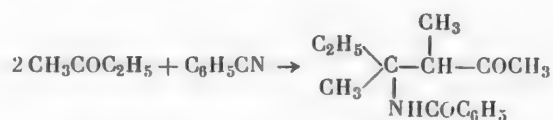


A point in favor of the first of the schemes presented is the capacity of aliphatic aldehydes, especially formaldehyde [4] and, as we showed in the present work, benzaldehyde, for conversion under the conditions of the Ritter reaction into the corresponding alkylidenebisamides, in all probability through the stage of hydroxy-alkylamide formation.



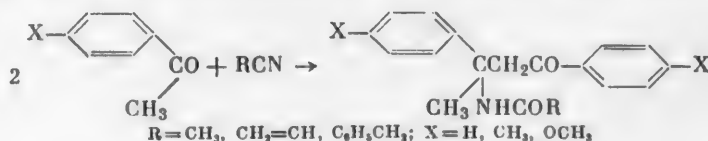
However, analogous conversions for ketones are unknown. Moreover, many examples of the condensation of nitriles with alcohols [1] and olefins by the Ritter reaction are known and the conditions we used corresponded to typical conditions for this reaction. Since there was no information on the application of the Ritter reaction to α,β -unsaturated ketones and the β -hydroxy ketones up to the beginning of our investigation, to confirm the possibility of an amide condensation of ketones by the second scheme, we studied the reaction of mesityl oxide and diacetone alcohol with benzonitrile under the conditions of the Ritter reaction and obtained the same 4-methyl-4-benzamidopentanone-2, described above, in yields of 78 and 37%. Simultaneously with this communication, [5] appeared in which the same reaction was described but with worse results. Since the reaction found was of specific interest, making it very simple to prepare extremely difficultly accessible acylamino ketones with branched chains, which are of interest as starting materials for the synthesis of certain substances with possible physiological activity, we carried out work to determine the limits of this reaction. For this purpose we investigated the condensation of ketones and nitriles of various structures under standard conditions, namely, in the presence of 96% sulfuric acid. The use of more dilute sulfuric acid led to a sharp fall in yields and the use of a solvent (acetic acid or dibutyl ether) gave a completely negative result. The use of 100% sulfuric acid and low-percent oleum as condensing agents led to considerable tar formation in the reaction mixture. It was found that though the reaction we discovered is not a general one, it may be used quite widely.

Acetone also reacted with acetonitrile but not with benzyl cyanide. Methyl ethyl ketone reacted with benzonitrile to form a single condensation product to which should be ascribed the structure of 3,4-dimethyl-4-benzamidohexanone-2 since the substance gave a positive iodoform reaction. The unequivocal nature of the reaction is in accord with literature data as it is known [6] that in an acidic medium methyl ethyl ketone gives only the product of condensation through the ethyl group.



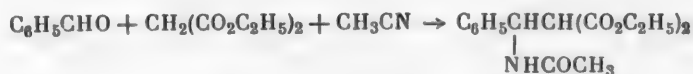
Butyrene and pinacoln did not condense with benzonitrile. The data presented show that positive results are given by ketones that undergo a condensation of the aldol-crotonic type especially readily. Ketones which are more inert in this respect give low yields or completely negative results since before the condensation occurs,

the nitrile disappears due to the competing reaction of hydrolysis to the amide. Among cyclic ketones, only cyclohexanone gives condensation products with nitriles. Other alicyclic ketones (cyclopentanone, α -tetralone, indanone-1, and camphor) do not react. Acetophenone and its substituted analogs (p-methyl- and p-methoxyacetophenone) give high yields of condensation products with acetonitrile, benzyl cyanide, and even acrylonitrile.



Nonetheless, acetophenones do not react with aromatic nitriles (benzonitrile, 2-methoxybenzonitrile, and α -naphthonitrile) or with di- and trichloroacetonitrile. Evidently, the highly active chlorine-substituted acetophenones are hydrolyzed more rapidly than the crotonic condensation products of acetophenones are formed. Together with this, the double bond of the dypones formed is evidently insufficiently active to react with the less active aromatic nitriles. Propiophenone does not react with nitriles under the conditions we chose. Thus, it can be seen that among the nitriles the best results are given by acetonitrile and slightly worse ones by benzonitrile, which reacts only with highly active ketones. Among the ketones, the best results are given by methyl ketones (acetone and acetophenone); with an increase in the size of the alkyl radical, the yields fall (methyl ethyl ketone) or completely negative results are obtained (propiophenone and butyrene). The results obtained could probably be improved partially if attempts were made to select specific reaction conditions for each individual case as we used standard conditions for comparison of the results.

Regardless of which of the two mechanisms presented above is the one by which the reaction proceeds, one molecule of carbonyl compound always reacts through its carbonyl group and the other through an α -methylene unit. In this connection we carried out a "cross" reaction where the compound with the active methylene unit was not a ketone, but another compound. We actually found that this reaction occurred when the carbonyl component was not a ketone, but an aldehyde; benzaldehyde and malonic ester condensed with acetonitrile in the presence of concentrated sulfuric acid to give a good yield of the ethyl ester of 1-carbethoxy-2-phenyl-2-acetamidopropionic acid.



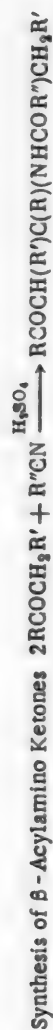
The latter variant of the reaction is also of undoubted interest for the synthesis of β -acylamino acids.

EXPERIMENTAL

β -Acylamino ketones. To a mixture of 0.2 mole of ketone and 0.1 mole of nitrile was added 11 ml of concentrated sulfuric acid (d 1.84) dropwise with stirring while the temperature of the reaction mixture was not allowed to rise above 25°. After a few days, the mixture was poured into a saturated aqueous solution of potassium or sodium carbonate. The precipitated crystalline substance was collected, dried, and then purified by recrystallization. Oily substances formed were extracted with ether and vacuum distilled. The substances obtained by this method, their characteristics, and also the reaction times are given in the table.

Hydrolysis of 2-(1'-benzamidocyclohexyl)-cyclohexanone. A mixture of 2.5 g of amido ketone and 20 ml of 5% hydrochloric acid was boiled in a flask attached to a distillation condenser until all the cyclohexanone had steam distilled. To the distillate was added semicarbazide carbonate and methanol until a homogeneous solution was formed. The precipitate of semicarbazone was recrystallized from methanol; it had m. p. 165-166°. A mixed melting point with an authentic sample of the semicarbazone of cyclohexanone was not depressed. Benzoic acid (m. p. 121.5-122°) recrystallized from the reaction mixture on cooling; a mixed melting point with an authentic sample was not depressed.

Condensation of mesityl oxide with benzonitrile. In a 3-day reaction, 9.8 g of ketone and 11 ml of benzonitrile in the presence of 5.5 ml of sulfuric acid (d 1.84) yielded 17 g (78%) of 4-methyl-4-benzamidopentanone-2 with m. p. 99-100°.



R	R'	R''	Reaction time (in days)	Yield (in %)	Melting point (recrystallization solvent)	Found (%)			Empirical formula	Calculated (%)	
						C	H			C	H
CH ₃	H	CH ₃	6	23	44–45°; b.p. * 104–106° (4 mm)	—	—	—	—	—	—
CH ₃	H	C ₆ H ₅	7	62	99.5–100.5 **	—	—	—	—	—	—
C ₂ H ₅	H	C ₆ H ₅	7	16	77–74 (Ligroline)	70.49, 70.59	8.61, 8.53	—	C ₁₅ H ₂₁ O ₂ N	70.01	8.23
C ₆ H ₅	H	CH ₃	4	74	93–94 (Cyclohexane)	77.03, 77.23	6.88, 6.79	—	C ₁₈ H ₁₉ O ₂ N	76.86	6.81
C ₆ H ₅	H	C ₆ H ₅ CH ₂	3	84	86–87 (Cyclohexane)	80.46, 80.53	6.54, 6.61	—	C ₂₄ H ₂₅ O ₂ N	80.63	6.48
C ₆ H ₅	H	CH ₂ =CH	2	54	120–121 (Ethanol)	77.74, 77.71	6.65, 6.59	—	C ₁₉ H ₁₉ O ₂ N	77.79	6.53
n-CH ₃ C ₆ H ₄	H	CH ₃	5	86	124–125 (Cyclohexene)	77.66, 77.76	7.67, 7.64	—	C ₂₀ H ₂₃ O ₂ N	77.83	7.49
n-CH ₃ OC ₆ H ₄	H	CH ₃	2	67	88–89 (Ethyl acetate + ligroline)	70.02, 70.06	6.83, 6.82	—	C ₂₀ H ₂₃ O ₄ N	70.36	6.79
Cyclohexanone		CH ₃	2	72	139–140 *** (Ligroline)	—	—	—	—	—	—
Cyclohexanone		C ₆ H ₅	2	51	118.5–119.5 (Ethyl acetate + ligroline)	76.56, 76.55	8.58, 8.40	—	C ₁₉ H ₂₅ O ₂ N	76.26	8.82

* Literature data [8]: B. p. 93–97° (1 mm); m. p. 46°.

** Literature data [2]: M. p. 101° (see also experiment on condensation of mesityl oxide and diacetone alcohol with benzonitrile).

*** Literature data [3]: M. p. 140–141°.

Condensation of diacetone alcohol with benzonitrile. Under analogous conditions 11.6 g of ketol, 0.1 mole of nitrile, and 11 ml of sulfuric acid (d 1.84) yielded 8.1 g (37%) of amido ketone with m. p. 99-100°. Mixed melting points of all the samples of 4-methyl-4-benzamidopentanone-2 obtained and also the product of benzoylating diacetone amine by the Schotten-Baumann method [2] were not depressed.

Ethyl ester of 1-carbethoxy-2-phenyl-2-acetamidopropionic acid. To a mixture of 16 g of malonic ester, 13 g of benzaldehyde, and 5 ml of acetonitrile was added 11 ml of concentrated sulfuric acid. After 3 days the reaction mixture was treated with sodium carbonate solution and the liberated oil carefully washed with water and left for 2 days under a layer of pure water; the crystals formed were collected, dried, and recrystallized from ligroine (b.p. 40-70°). The yield was 18.2 g (55%) and the m. p. 81-82°.

Found %: C 62.76, 62.88; H 6.92, 7.04. $C_{16}H_{21}O_5N$. Calculated %: C 62.58; H 6.89.

The colorless platelets were readily soluble in ether, acetone, and benzene and difficultly soluble in ligroine.

Benzylidenebisacetamide. Benzaldehyde (6.5 g), 5 ml of acetonitrile, and 5 ml of concentrated sulfuric acid were mixed with cooling in ice water. After standing for 3 days at room temperature, the mixture was treated with sodium carbonate solution and the crystals liberated were recrystallized from ethanol. The yield was 9.1 g (78%) and the m. p. 241-242°. Literature data for benzylidenebisacetamide [7]: M. p. 240-241°.

Found %: C 64.48, 64.31; H 7.08, 7.01. $C_{11}H_{14}O_2N_2$. Calculated %: C 64.08; H 6.84.

SUMMARY

1. It was found that in the presence of concentrated sulfuric acid, ketones react with nitriles to form β -acylamino ketones with branched chains which were produced by condensation of two molecules of ketone with one molecule of nitrile. New data are presented on the determination of the limits of applicability of these new reactions.

2. A condensation of benzaldehyde with malonic ester was carried out to yield the ethyl ester of 1-carbethoxy-2-phenyl-2-acetamidopropionic acid.

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CYCLOSERINE AND RELATED COMPOUNDS

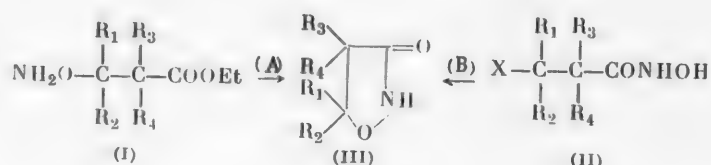
VIII. SYNTHESIS OF ISOXAZOLIDONES-3

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M. Ya. Karpeiskii, E. I. Budovskii, and V. I. Erashko

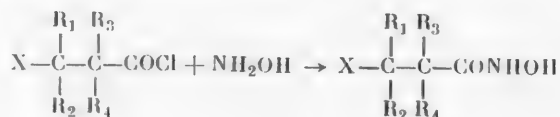
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In connection with investigations on the synthesis of cycloserine, a need arose for information on the chemical properties of a previously unknown heterocyclic system, isoxazolidone-3, which forms the basis of the antibiotic. Until now there has been no general method for synthesizing compounds of this type and the only known example of isoxazolidones-3, apart from cycloserine, was unsubstituted isoxazolidone-3. It was synthesized by cyclization of β -aminohydroxypropionic ester [1]. At the time when the present investigation was complete, an article appeared on a second synthesis of isoxazolidone-3 by cyclization of β -chloropropionhydroxamic acid [2]. To study the chemical properties of the isoxazolidone-3 system, it was necessary to have a general method of synthesizing the simplest representatives of this class, namely alkyl- and aryl-substituted isoxazolidones-3.

Of the two possible routes to the synthesis of the isoxazolidone system, cyclization of esters of β -amino-hydroxypropionic acids (Route A) or β -halopropionhydroxamic acids (Route B), the second one seemed more convenient.



This is due to the fact that it is apparently difficult to find any convenient and sufficiently general method of synthesizing the starting β -aminohydroxy substituted propionic acids (I). For synthesizing isoxazolidones-3 by the second route, it was necessary to develop a method of synthesizing β -halo substituted hydroxamic acids (II), which were unknown at the beginning of our work. The difficulty arising in this synthesis was that during the action of hydroxylamine on esters of β -halo substituted acids, hydrogen halide was eliminated. In order to overcome this difficulty, we reacted β -halo substituted acid chlorides with hydroxylamine at low temperature. Under these conditions the lability of the acid chloride chlorine atom so exceeded the activity of the β -halo atom that hardly any dehydrohalogenation occurred and this reaction was a convenient and sufficiently general method of synthesizing β -halo substituted hydroxamic acids.

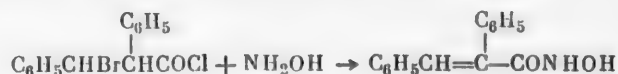


We used this method to obtain 50-60% yields of β -chloropropionhydroxamic (II, $R_1, R_2, R_3, R_4 = H, X = Cl$), β -bromopropionhydroxamic (II, $R_1, R_2, R_3, R_4 = H, X = Br$), β -bromoisobutyrohydroxamic (II, $R_1, R_2, R_3 = H, R_4 = CH_3, X = Br$), β -chloroisovalerohydroxamic (II, $R_3, R_4 = H, R_1, R_2 = CH_3, X = Cl$), and β -bromo- β -phenylpropionhydroxamic (II, $R_1, R_3, R_4 = H, R_2 = C_6H_5, X = Br$) acids. The method developed was also applied to the synthesis of

α,β -dihalopropionhydroxamic acids, which were also previously unknown and which could be interesting for the synthesis of functionally substituted isoxazolidones-3. Reaction of acid chlorides of α,β -dichloro- and α,β -dibromopropionic acids with hydroxylamine gave 50-60% yields of α,β -dichloropropionhydroxamic (II, $R_1, R_2, R_3 = H, X, R_4 = Cl$) and α,β -dibromopropionhydroxamic (II, $R_1, R_2, R_3 = H, X, R_4 = Br$) acids. The halo-substituted hydroxamic acids obtained were stable, crystalline substances, giving a characteristic reaction with ferric chloride solution.

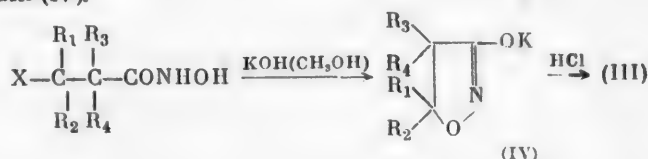
After we had developed this method of synthesizing halo-substituted hydroxamic acids [3], communication [2] appeared on the synthesis of one representative of this class, β -chloropropionhydroxamic acid, by an analogous method.

In only one case were we unable to obtain the desired result. In an attempt to prepare β -bromo- α,β -diphenylpropionhydroxamic acid by reaction of β -bromo- α,β -diphenylpropionyl chloride with hydroxylamine, despite variation of the conditions, only the corresponding unsaturated hydroxamic acid was isolated.



Evidently the presence of two phenyl nuclei promoted dehydrobromination to such an extent that it was practically impossible to avoid it.

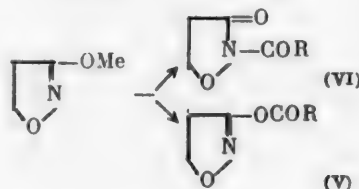
To prepare isoxazolidones-3 (III), we made a detailed study of the cyclization of halo-substituted hydroxamic acids (II) under the action of alkaline agents. With cyclization by the action of aqueous solutions of caustic alkalis, as recommended in recently published work on the synthesis of isoxazolidone-3 from β -chloropropionhydroxamic acid [2], we were unable to obtain positive results. Although isoxazolidones were formed, as indicated by a positive qualitative sodium nitroprusside test [4], we were unable to isolate them in a crystalline state. In addition, under these conditions the reaction did not proceed in one direction as substances were simultaneously formed which had higher melting points than isoxazolidones and did not give a color with nitroprusside. We obtained positive results by cyclizing β -halo substituted hydroxamic acids with a methanol solution of potassium hydroxide. In this case isoxazolidones-3 were formed in about 70% yield and could be isolated readily from the reaction mixture in the form of potassium salts (IV).



In this way we obtained the potassium salts of isoxazolidone-3 (IV, $R_1, R_2, R_3, R_4 = H$), 4-methylisoxazolidone-3 (IV, $R_1, R_2, R_3 = H, R_4 = \text{CH}_3$), 5-phenylisoxazolidone-3 (IV, $R_2, R_3, R_4 = H, R_1 = \text{C}_6\text{H}_5$) and 5,5-dimethylisoxazolidone-3 (IV, $R_3, R_4 = H, R_1, R_2 = \text{CH}_3$), and the nature of the halogen in the β -position had no noticeable effect on the yield of the isoxazolidone-3. Treatment of the potassium salts with silver nitrate in aqueous solution readily formed the silver salts of the corresponding isoxazolidones-3. By treatment of solutions of the potassium salts in anhydrous alcohol with the calculated amount of hydrogen chloride, we isolated isoxazolidones (III) as colorless, crystalline substances in about 70% yield. Only one of these compounds, namely, 5,5-dimethylisoxazolidone-3 (III, $R_3, R_4 = H, R_1, R_2 = \text{CH}_3$), could not be obtained in a crystalline form and purified. Thus, cyclization of β -halo substituted hydroxamic acids under the action of a methanol solution of potassium hydroxide was a convenient and sufficiently general method of synthesizing isoxazolidones-3.

We also attempted to cyclize α,β -dihalopropionhydroxamic acids. This reaction could be of considerable interest as it would make it possible to obtain 4-haloisoxazolidones-3 and from them, 4-substituted isoxazolidones-3, i.e., the closest analogs of cycloserine. However, despite many attempts at cyclization under the action of various agents and under various conditions, positive results were not obtained. In all cases the reaction proceeded in a different direction with the evolution of gaseous products and was evidently accompanied by complete decomposition of the dihalohydroxamic acids. In the cyclization of the γ -halobutyrohydroxamic acids we obtained, N-hydroxypyrrolidones were formed instead of the corresponding oxazin-1,2-ones-3.

Of the chemical properties of the isoxazolidones-3 obtained, we have as yet studied only their acylation on the example of unsubstituted isoxazolidone-3. There is a brief report [5], that acetylation of cycloserine gives a mixture of acetyl derivatives and therefore, the acetylation of isoxazolidone-3 is of interest. In the benzylation of isoxazolidone-3 under the conditions of the Schotten-Baumann reaction, we observed the formation of acylation products; however, the yields were very low and it was impossible to isolate the products in an analytically pure state. A study was then made of the benzylation of metal derivatives of isoxazolidone-3, namely, its potassium and silver salts. Leaving on one side the problem of the true structure of these salts, which could be of the N-Me or O-Me type, before a special investigation we considered that the process could lead to the formation of an O- (V) or N-benzoyl (VI) derivative or a mixture of the two.



Treatment of either the potassium or the silver salt of isoxazolidone-3 with benzoyl chloride in aqueous dioxane at room temperature gave a 40-50% yield of only one crystalline benzoyl derivative with m. p. 123-124°. The problem of the structure of the compound obtained was solved by means of its infrared and ultraviolet spectra.*

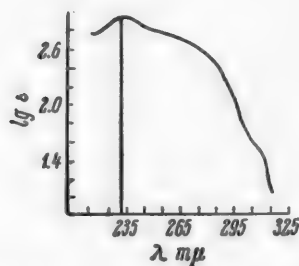


Fig. 1. Ultraviolet spectrum of N-benzoylisoxazolidone-3 ($c = 10^{-3}$, in methanol).

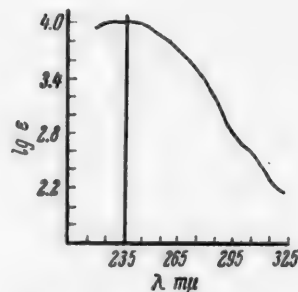


Fig. 2. Ultraviolet spectrum of the α -form of trisubstituted hydroxylamine ($c = 2 \cdot 10^{-3}$, in methanol).

In the carbonyl frequency region, the infrared spectrum contained two absorption bands, indicating the presence of two carbonyl groups. The band at 1698 cm^{-1} is the amide band of a carbonyl in a heterocyclic system; the band at 1770 cm^{-1} indicates the presence of an aromatic carbonyl. No absorption bands were detected in the region of double bond frequencies ($1620\text{-}1640 \text{ cm}^{-1}$). These data support structure (VI) for the benzoyl derivatives of isoxazolidone-3. This conclusion was also confirmed by the nature of the ultraviolet spectrum (see Fig. 1). The spectra of the compound obtained were similar to those of the α -form of trisubstituted hydroxylamine (see Fig. 2) [6], which also indicates the presence of the grouping $\text{O}=\text{C}-\text{N}-\text{COC}_6\text{H}_5$ in the compound we obtained



and supports structure (VI).

Thus, both the potassium and silver salts of isoxazolidone-3 gave the same N-benzoyl derivative.

We also acylated the potassium salt of isoxazolidone-3 with p-nitrobenzoyl chloride and methyl chloro-carbonate under the same conditions. In both cases we obtained crystalline substances, which, by analogy, we considered to be N-acyl derivatives (VI) ($\text{R} = \text{p-NO}_2\text{C}_6\text{H}_4$ or CH_3CO). The result obtained by studying acylation reaction, in addition to its value in the chemistry of isoxazolidones and cycloserine, is also interesting theoretically.

* The ultraviolet spectra were plotted in the laboratory of the Pharmacology Institute and the infrared spectra in the laboratory of the Chemistry Faculty of Moscow State University. The authors are very grateful to V. G. Vinokurova and L. A. Kazitsina who did this work.

As is well-known [7], for metallic derivatives of similar systems, replacement often depends on the nature of the metal. In the benzoylation of isoxazolidone-3 the reaction proceeds in the same direction in both cases. This indicates interesting characteristics of the new heterocyclic system, isoxazolidone-3, which is a cyclic O-ester of hydroxamic acid.

EXPERIMENTAL

Preparation of Halo-Substituted Hydroxamic Acids

β -Bromopropionhydroxamic acid. A solution of 32 g of sodium hydroxide in 120 ml of water was cooled to 0° and 55.5 g of hydroxylamine hydrochloride added. With vigorous stirring at a temperature of no higher than +5°, to the solution obtained was added 68.6 g of freshly distilled β -bromopropionyl chloride. The reaction mixture was then stirred for 1 hour at 0-5° and 1.5 hours at 15°, heated to 60°, and filtered. The filtrate was kept at -5° for 30-48 hours, when it deposited a precipitate, which was collected and recrystallized from hot water; it had m. p. 88-90°. The yield was 33-34 g (48-50%).

Found %: C 21.54; H 3.67; N 8.29. $C_3H_6O_2NBr$. Calculated %: C 21.43; H 3.57; N 8.33.

β -Chloropropionhydroxamic acid. Under analogous conditions, 24 g of sodium hydroxide, 42 g of hydroxylamine hydrochloride in 100 ml of water, and 38.1 g of β -chloropropionyl chloride yielded 18.5-20 g (50-55%) of substance with m. p. 102-104° (from water).

Found %: N 13.31; Cl 28.67. $C_3H_5O_2NCl$. Calculated %: N 13.35; Cl 28.69.

β -Bromoisobutyrohydroxamic acid. To a solution of 5.6 g of sodium hydroxide and 9.7 g of hydroxylamine hydrochloride in 20 ml of water, cooled to -12°, was added 13 g of β -bromo- α -methylpropionyl chloride with stirring. The reaction mixture was stirred for 1.5 hours at -10° and 2 hours at +10°. The precipitate was collected, washed with ether, and recrystallized from water. We obtained 6.5-7 g of substance (52-55%) with m. p. 98-100°.

Found %: N 6.98; Br 43.90. $C_4H_8O_2NBr$. Calculated %: N 7.38; Br 43.96.

β -Bromo- β -phenylpropionhydroxamic acid. A solution of 4.8 g of sodium hydroxide and 8.4 g of hydroxylamine hydrochloride in 20 ml of water was cooled to -25°, 15 g of β -bromo- β -phenylpropionyl chloride added, and the mixture stirred for 1.5 hours at -15°. The precipitate was rapidly collected and dried in vacuum over alkali. We obtained 9 g (61%) of an extremely hygroscopic substance with m. p. 85-90°. The substance could not be recrystallized and it was used in subsequent reactions without further purification.

β -Chloroisovalerohydroxamic acid. This compound was obtained under the same conditions from 13.2 g of sodium hydroxide, 22.8 g of hydroxylamine hydrochloride in 40 ml of water, and 22.5 g of β -chloroisovaleryl chloride. After the reaction mixture had been stirred for 1.5 hours at -15°, the precipitated oil was separated, dissolved in 100 ml of ether, and filtered from the precipitate. The ether solution was evaporated without heating and the residue dried in vacuum over phosphorous pentoxide. We obtained 16 g (65%) of β -chloroisovalerohydroxamic acid as a yellow, uncrystallizable oil, which was then used without further purification.

α,β -Diphenylacrylhydroxamic acid. Under analogous conditions 4.5 g of hydroxylamine hydrochloride and 2.6 g of sodium hydroxide in 15 ml of water and 10.5 g of β -bromo- α,β -diphenylpropionic acid in 10 ml of dioxane yielded 4.6 g (50%) of α,β -diphenylacrylhydroxamic acid with m. p. 147-149° (from dry dichloroethane).

Found %: C 75.07; H 5.21; N 5.64. $C_{15}H_{13}O_2N$. Calculated %: C 75.31; H 5.44; N 5.85.

α,β -Dibromopropionhydroxamic acid. To a solution of 16 g of sodium hydroxide and 28 g of hydroxylamine hydrochloride in 50 ml of water was added 50 g of α,β -dibromopropionyl chloride with stirring and cooling to 0° and then the reaction mixture was stirred for 1 hour at 0° and 1.5 hours at 15-18°, heated to boiling, and filtered. On cooling, the filtrate deposited 27-30 g (55-60%) of a substance with m. p. 151-153° (from water).

Found %: N 5.49. $C_3H_5O_2NBr_2$. Calculated %: N 5.67.

α,β -Dichloropropionhydroxamic acid. This compound was obtained analogously from 16 g of sodium hydroxide and 27.8 g of hydroxylamine hydrochloride in 50 ml of water and 32.3 g of α,β -dichloropropionyl chloride. The yield was 18-19 g (50-60%) and the m. p. 95-97° (from water).

Found %: N 8.71. $C_3H_5O_2NCl_2$. Calculated %: N 8.85.

Preparation of Isoxazolidone-3 and its Homologs

Isoxazolidone-3. To a solution of 6.8 g of β -bromopropionhydroxamic acid in 15 ml of anhydrous methyl alcohol was added 40 ml of a 2 N methanol solution of potassium hydroxide and the reaction mixture heated for 40 minutes. The precipitate of potassium bromide was removed by filtration and the filtrate evaporated in vacuum without heating. The residue was dissolved in a small amount of anhydrous alcohol, the insoluble residue removed by filtration, and the filtrate again evaporated to dryness in vacuum without heating. When triturated with absolute ether, the residual oil changed completely into a crystalline substance which was dried in vacuum over alkali and phosphorous pentoxide and reprecipitated from butyl alcohol with ether. We obtained 18-19 g (80-85%) of the crystalline potassium salt of isoxazolidone-3 with m. p. 213-215° (decomp.).

Found %: N 11.20. $C_3H_4O_2NK$. Calculated %: N 11.20.

A portion of 3.75 g of the potassium salt of isoxazolidone-3 was dissolved in 10 ml of water and 240 ml of 0.1 N silver nitrate solution added. The precipitate was collected and dried in a vacuum desiccator over alkali. We obtained 5-5.2 g (86-89%) of the silver salt of isoxazolidone-3 with m. p. 166-168° (decomp.).

Found %: C 18.34; H 1.99; N 7.42. $C_3H_4O_2NAg$. Calculated %: C 18.56; H 2.06; N 7.22.

A sample of 1.25 g of the potassium salt of isoxazolidone-3 was dissolved in 20 ml of anhydrous alcohol and 0.365 g of hydrogen chloride in anhydrous alcohol added. The potassium chloride precipitate was removed by filtration, 200 ml of absolute ether added to the filtrate, and the solution filtered and evaporated to dryness without heating. We obtained 0.6 g (70%) of isoxazolidone-3 with m. p. 69-70°.

Found %: N 15.95. $C_3H_5O_2N$. Calculated %: N 16.08.

Literature data [2]: m. p. 68-70°.

4-Methylisoxazolidone-3. Similarly 6.7 g of β -bromo- α -methylpropionhydroxamic acid in 20 ml of anhydrous methyl alcohol and 37 ml of 2 N methyl alcohol solution of potassium hydroxide yielded 3.6 g (70%) of the crystalline potassium salt of 4-methylisoxazolidone-3, which had m. p. 151-153° (decomp.) after reprecipitation from isopropyl alcohol with ether.

Found %: C 34.62; H 4.72; N 9.91. $C_4H_6O_2NK$. Calculated %: C 34.53; H 4.32; N 10.07.

Under the same conditions, 2 g of the potassium salt and 0.365 g of hydrogen chloride in anhydrous alcohol yielded 4-methylisoxazolidone-3 as an oil. The oil obtained was dried in vacuum over phosphorous pentoxide, dissolved in anhydrous isopropyl alcohol, and the solution treated with absolute ether with cooling and stirring. The hygroscopic crystals liberated were again dried in vacuum over phosphorous pentoxide. The yield of 4-methylisoxazolidone-3 was 1.1 g (70%) and the m. p. 72-74° (decomp.).

Found %: N 13.56. $C_4H_7O_2N$. Calculated %: N 13.86.

5-Phenylisoxazolidone-3. Under analogous conditions, 3.7 g of β -bromo- β -phenylpropionhydroxamic acid in 20 ml of anhydrous methyl alcohol and 15 ml of a 2 N solution of potassium hydroxide in methyl alcohol yielded 2.8 g of crystalline potassium salt of 5-phenylisoxazolidone-3. Two reprecipitations from anhydrous methyl alcohol with ether yielded 2.1 g (70%) of potassium salt with m. p. 285-287° (decomp.).

Found %: C 53.48; H 4.05. $C_9H_8O_2NK$. Calculated %: C 53.73; H 3.98.

Under analogous conditions, 1 g of the potassium salt of 5-phenylisoxazolidone-3 yielded 0.6 g of crystalline 5-phenylisoxazolidone-3. Recrystallization from anhydrous alcohol yielded 0.5 g (62%) of a substance with m. p. 121-123°.

Found %: N 8.24. $C_9H_9O_2N$. Calculated %: N 8.58.

5,5-Dimethylisoxazolidone-3. From 11 g of the oily β -chloroisovalerohydroxamic acid in 30 ml of anhydrous methyl alcohol and 72 ml of 2 N potassium hydroxide solution, under analogous conditions, we obtained 8 g of a thick oil, which crystallized almost completely after prolonged trituration with ether and many solvent changes (up to 20). Drying in vacuum over phosphorous pentoxide and alkali and reprecipitation from methyl alcohol with absolute ether yielded 5 g (50%) of the very hygroscopic, crystalline potassium salt of 5,5-dimethylisoxazolidone-3 with m. p. 122-125°.

Found %: N 8.93. $C_5H_9O_3NK$. Calculated %: N 9.20.

From 1.53 g of the potassium salt of 5,5-dimethylisoxazolidone-3 and 80 ml of 0.1 N silver nitrate solution we obtained 1.9 g (85%) of the silver salt of 5,5-dimethylisoxazolidone-3 with m. p. 166-168° (decomp.).

Found %: N 5.81. $C_5H_9O_3NAg$. Calculated %: N 6.27.

An attempt to prepare 5,5-dimethylisoxazolidone-3 from its potassium salt by the method described above yielded an oily substance, which could not be purified and crystallized.

N-Benzoylisoxazolidone-3. A. A solution of 1.4 g of benzoyl chloride in 10 ml of dioxane was added dropwise with stirring to 1.25 g of the potassium salt of isoxazolidone-3 in 10 ml of dioxane. The mixture was stirred for 2 hours at room temperature, the potassium chloride removed by filtration, and the filtrate evaporated to dryness at a bath temperature of no higher than 60°. The residue was 1.4 g of a yellow oil which crystallized almost completely when triturated with absolute ether. The substance obtained was dried in vacuum over alkali and recrystallized from aqueous dioxane (1 : 1) to give 0.9 g (47%) of N-benzoylisoxazolidone-3 with m. p. 123-124°.

Found %: C 63.20; H 4.88. $C_{10}H_9O_3N$. Calculated %: C 62.88; H 4.71.

B. To a mixture of 1.94 g of the silver salt of isoxazolidone-3 and 10 ml of dioxane was added a solution of 1.4 g of benzoyl chloride in 10 ml of dioxane with stirring. The mixture was stirred for 3 hours at room temperature, the silver chloride precipitate removed by filtration, and the filtrate evaporated to dryness at a bath temperature no higher than 60°. The residue was 1.8 g of a yellow oil which crystallized almost completely when triturated with dry ether. Appropriate treatment yielded 0.75 g (40%) of the crystalline benzoyl derivative of isoxazolidone-3 with m. p. 123-124°. A mixed melting point with the sample obtained in the previous experiment was not depressed.

N-(p-Nitrobenzoyl)-isoxazolidone-3. A solution of 0.93 g of p-nitrobenzoyl chloride in 10 ml of dioxane was added with stirring to a mixture of 0.6 g of the potassium salt of isoxazolidone-3 and 10 ml of dioxane. The mixture was stirred at room temperature for 2 hours and then treated as described above to yield 2 g of a crystalline substance, which was recrystallized from aqueous dioxane (2 : 1). We obtained 1.2 g (51%) of a substance with m. p. 178-180°.

Found %: N 11.02. $C_{10}H_9O_3N_2$. Calculated %: N 11.32.

N-Carbomethoxyisoxazolidone-3. To a mixture of 1.25 g of the potassium salt of isoxazolidone-3 and 30 ml of dioxane was added 0.95 g of methyl chlorocarbonate in one portion with stirring. The reaction mixture was stirred at 50-55° for 4 hours. Treatment as described above gave a residue of 1.2 g of oil, which crystallized almost completely after prolonged trituration with absolute ether and alcohol. Drying the substance in vacuum over phosphorous pentoxide and recrystallization from isopropyl alcohol gave 0.6 g (40%) of a crystalline substance with m. p. 106-108°.

Found %: N 9.44. $C_6H_7O_4N$. Calculated %: N 9.67.

SUMMARY

1. A general method was developed for synthesizing β -halo and α,β -dihalo substituted hydroxamic acids by the reaction of acid chlorides of appropriate aliphatic acids with hydroxylamine (base) in an aqueous medium.
2. A general method was developed for synthesizing alkyl- and arylisoxazolidones-3 by cyclization of β -halo substituted hydroxamic acids with methanol solution of potassium hydroxide.
3. The acylation of isoxazolidone-3 by benzoyl chloride, p-nitrobenzoyl chloride, and methyl chlorocarbonate was studied.
4. It was shown that benzoylation of the potassium and silver salts of isoxazolidone-3 formed the same N-benzoyl derivative.

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DIARYL ESTERS OF N-PHOSPHORIC ACIDS OF AMIDINES OF THE AROMATIC SERIES

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C-Chloro-P,P-diaroxysophosphazaroaroyls [1] were recently prepared according to the scheme



In previous work [1, 2] it was shown that the halogen in these compounds is readily replaced by hydroxyl and aroxyl; the Arbuzov reaction also proceeds readily [3].

The action of ammonia, diethylamine, and aniline on C-chloro-P,P-diaroxysophosphazaroaroyls formed diaryl esters of N-phosphoric acids of amidines (I), N',N'-diethylamidines (II), and N'-phenylamidines (III) and (IV) of the aromatic series by the scheme



With ammonia and diethylamine the reaction proceeded very readily with strong heat evolution, while with aniline it proceeded more slowly and was completed only by boiling in benzene or chlorobenzene.

The diaryl esters of N-phosphoric acids of aromatic amidines were colorless, crystalline substances (see table) which were insoluble in water and did not distill without decomposition. Substances (I) and (II) were quite readily soluble in organic solvents, while (III) and (IV) were much more difficultly soluble (see experimental section).

The basic properties of the diaryl esters of N-phosphoric acids of amidines were expressed extremely weakly — they did not give salts with strong acids in aqueous solutions, but the action of dry hydrogen chloride in benzene converted them into salts, which were clear, colorless, glassy masses that were quantitatively converted into the starting diaryl esters of N-phosphoric acids of the corresponding amidines by treatment with weak alkali.

When substances (I) were heated in aqueous alcohol in the presence of strong acids, they polymerized, while (II) and (III) were unchanged under the same conditions. Evidently the presence of two hydrogen atoms on the nitrogen atoms was necessary for polymerization.

On thermal cleavage, substances (I) and (II) decomposed to nitriles of carboxylic acids and amides of phosphoric diesters by the scheme



The reaction proceeded at lower temperatures and with higher yields for substances (II) than for (I) and this is apparently explained by the lower stability of the amide of diphenyl phosphate as compared with the phenylamide of diphenyl phosphate.

Diaryl Esters of N-Phosphoric Acids of Aromatic Amidines of the Type $\text{Ar}(\text{NRR}') = \text{NPQ}(\text{OAr}')_2$

Ar	R	R'	Ar'	Yield (in %)	Melting point	External form: recrystallization solvent	N found (%)	Empirical formula	N calculated (%)
(I) $\left\{ \begin{array}{l} \text{C}_6\text{H}_5 \\ \text{p-ClC}_6\text{H}_4 \\ \text{p-NO}_2\text{C}_6\text{H}_4 \\ \text{m-NO}_2\text{C}_6\text{H}_4 \\ 3,5-(\text{NO}_2)_2\text{C}_6\text{H}_3 \\ \text{C}_6\text{H}_5 \end{array} \right\}$	H	H	C_6H_5	99	99—101°	Needles, alcohol	8.15	$\text{C}_{19}\text{H}_{17}\text{O}_3\text{N}_2\text{P}$	7.95
	H	H	C_6H_5	96	147—149	The same	7.23	$\text{C}_{19}\text{H}_{16}\text{O}_3\text{N}_2\text{P}$	7.24
	H	H	C_6H_5	98	168—170	"	10.67	$\text{C}_{19}\text{H}_{16}\text{O}_3\text{N}_3\text{P}$	10.57
	H	H	C_6H_5	100	128—130	Plates, alcohol	10.77	$\text{C}_{19}\text{H}_{16}\text{O}_3\text{N}_3\text{P}$	10.57
	H	H	C_6H_5	93	182—183	Needles, alcohol	12.68	$\text{C}_{19}\text{H}_{15}\text{O}_7\text{N}_4\text{P}$	12.67
(II) $\left\{ \begin{array}{l} \text{C}_6\text{H}_5 \\ \text{p-ClC}_6\text{H}_4 \\ \text{p-NO}_2\text{C}_6\text{H}_4 \\ \text{m-NO}_2\text{C}_6\text{H}_4 \\ 3,5-(\text{NO}_2)_2\text{C}_6\text{H}_3 \end{array} \right\}$	H	H	$\alpha\text{-C}_{10}\text{H}_7$	90	119—121	Prisms, alcohol	6.37	$\text{C}_{27}\text{H}_{31}\text{O}_3\text{N}_2\text{P}$	6.17
	C_2H_5	C_2H_5	C_6H_5	98	77—79	Plates, ligroine	6.95	$\text{C}_{23}\text{H}_{25}\text{O}_3\text{N}_2\text{P}$	6.85
	C_2H_5	C_2H_5	C_6H_5	91	69—71	Plates, benzene	6.47	$\text{C}_{23}\text{H}_{24}\text{O}_3\text{N}_2\text{P}$	6.32
	C_2H_5	C_2H_5	C_6H_5	73	102—104	Needles, ligroine	9.27	$\text{C}_{23}\text{H}_{24}\text{O}_5\text{N}_3\text{P}$	9.26
	C_2H_5	C_2H_5	C_6H_5	91	100—102	The same	9.56	$\text{C}_{23}\text{H}_{24}\text{O}_5\text{N}_3\text{P}$	9.26
(III) $\left\{ \begin{array}{l} \text{C}_6\text{H}_5 \\ \text{p-ClC}_6\text{H}_4 \\ \text{p-NO}_2\text{C}_6\text{H}_4 \\ \text{m-NO}_2\text{C}_6\text{H}_4 \\ 3,5-(\text{NO}_2)_2\text{C}_6\text{H}_3 \end{array} \right\}$	C_2H_5	C_2H_5	C_6H_5	90	99—100	Clusters of needles, ligroine + CCl_4	11.15	$\text{C}_{23}\text{H}_{23}\text{O}_7\text{N}_4\text{P}$	11.24
	C_6H_5	H	C_6H_5	65	153—155	Prisms, dioxane	6.47	$\text{C}_{25}\text{H}_{21}\text{O}_3\text{N}_2\text{P}$	6.53
	C_6H_5	H	C_6H_5	100	192—193	Prisms, benzene	6.01	$\text{C}_{25}\text{H}_{20}\text{O}_3\text{N}_2\text{P}$	6.05
	C_6H_5	H	C_6H_5	76	195—196	Prisms, dioxane	8.87	$\text{C}_{25}\text{H}_{20}\text{O}_5\text{N}_3\text{P}$	8.87
	C_6H_5	H	C_6H_5	100	204—206	The same	8.47	$\text{C}_{25}\text{H}_{20}\text{O}_5\text{N}_3\text{P}$	8.87
(IV) $\left\{ \begin{array}{l} \text{C}_6\text{H}_5 \\ \text{p-ClC}_6\text{H}_4 \\ \text{p-NO}_2\text{C}_6\text{H}_4 \\ \text{m-NO}_2\text{C}_6\text{H}_4 \\ 3,5-(\text{NO}_2)_2\text{C}_6\text{H}_3 \end{array} \right\}$	C_6H_5	H	C_6H_5	100	164—165	Needles, methanol + ethanol	11.13	$\text{C}_{25}\text{H}_{19}\text{O}_7\text{N}_4\text{P}$	10.80
	C_6H_5	H	$\text{p-NO}_2\text{C}_6\text{H}_4$	63	153—155	Prisms, dioxane	10.81	$\text{C}_{25}\text{H}_{19}\text{O}_7\text{N}_4\text{P}$	10.80
	C_6H_5	H	$\text{p-NO}_2\text{C}_6\text{H}_4$	70	225—228	The same	10.31	$\text{C}_{25}\text{H}_{18}\text{O}_7\text{N}_4\text{P}$	10.14
	C_6H_5	H	$\text{p-NO}_2\text{C}_6\text{H}_4$	84	232—233	Prisms, dioxane + ethanol	12.25	$\text{C}_{25}\text{H}_{18}\text{O}_9\text{N}_5\text{P}$	12.43
	C_6H_5	H	$\text{p-NO}_2\text{C}_6\text{H}_4$	89	172—174	The same	12.26	$\text{C}_{25}\text{H}_{18}\text{O}_9\text{N}_5\text{P}$	12.43
	C_6H_5	H	$\text{p-NO}_2\text{C}_6\text{H}_4$	69	210—212	Needles, dioxane	13.61	$\text{C}_{25}\text{H}_{17}\text{O}_{11}\text{N}_6\text{P}$	13.81

EXPERIMENTAL

Diaryl esters of N-phosphoric acids of amidines of the type $\text{ArC}(\text{NH}_2) = \text{NPO}(\text{OAr}')_2$ (I). A solution of 0.02 mole of C-chloro-P,P-diaroxysophosphazoaroyl in 60 ml of dry benzene was treated with dry ammonia for 3 hours at such a rate that the temperature of the reaction mixture was kept within the range 20–30°. The flask was then stoppered and left at room temperature for 10–12 hours. The benzene was removed in vacuum and the solid, crystalline residue washed with warm water (3 × 20 ml), dried, and recrystallized from alcohol. All substances (I) were quite readily soluble in alcohol, benzene, and acetone, difficultly soluble in ether, ligroine, and carbon tetrachloride, and insoluble in water.

Diphenyl esters of N-phosphoric acids of N,N'-diethylamidines of the type $\text{ArC}(\text{N}(\text{C}_2\text{H}_5)_2) = \text{PO}(\text{OC}_6\text{H}_5)_2$ (II). With stirring and cooling, to a solution of 0.01 mole of C-chloro-P,P-diphenoxysophosphazoaroyl in 40 ml of anhydrous ether, cooled to 0°, was added a solution of 0.03 mole of diethylamine in 10 ml of anhydrous ether at such a rate that the temperature of the reaction mixture did not exceed 30°. After 24 hours, the ether was removed in vacuum and the crystalline residue washed with water (3 × 10 ml), dried, and recrystallized. All substances (II) were readily soluble in alcohol, benzene, and acetone, more difficultly so in ether, ligroine, and CCl_4 , and insoluble in water.

Diphenyl esters of N-phosphoric acids of N'-phenylamidines of the type $\text{ArC}(\text{NHC}_6\text{H}_5) = \text{NPO}(\text{OC}_6\text{H}_5)_2$ (III). With stirring and cooling, a solution of 0.02 mole of aniline in 15 ml of benzene was added to a solution of 0.01 mole of C-chloro-P,P-diphenoxysophosphazoaroyl in 50 ml of dry benzene at such a rate that the temperature of the reaction mixture did not exceed 30° and then the mixture was boiled for 2 hours under reflux. The benzene was removed in vacuum and the crystalline residue washed with hot water (3 × 20 ml), dried in air, and recrystallized. All the substances (III) were difficultly soluble in acetone, benzene, ether, alcohol, CCl_4 , and ligroine, insoluble in water, and quite readily soluble in dioxane.

Di-p-nitrodiphenyl esters of N-phosphoric acids of N'-phenylamidines of the type $\text{ArC}(\text{NHC}_6\text{H}_5) = \text{NPO}(\text{OC}_6\text{H}_4\text{NO}_2\text{-p})_2$ (IV). To a solution of 0.01 mole of C-chloro-P,P-dinitrodiphenoxysophosphazoaroyl in 50 ml of dry chlorobenzene was added 0.02 mole of aniline with stirring; this was accompanied by slight heat evolution. The mixture was boiled for 2 hours and cooled and the crystalline precipitate collected, washed with hot water, dried, and recrystallized. All substances (IV) were insoluble in water, difficultly soluble in the usual organic solvents, and slightly more soluble in boiling dioxane.

Thermal degradation of the diphenyl ester of the N-phosphoric acid of benzamidine. A sample of 0.01 mole of the diphenyl ester of the N-phosphoric acid of benzamidine was heated in a Claisen flask on an oil bath at a pressure of 0.3 mm. Decomposition began at a bath temperature of 270–280° and was complete in 5–6 minutes. A light yellow liquid (about 70% of the weight of the starting material) distilled and this partially crystallized rapidly; about 30% of a thick, viscous tar remained in the flask. The crystals were collected, washed with alcohol, and recrystallized from alcohol; they had m.p. 144–146° and did not depress the melting point of the amide of diphenyl phosphate; the yield was 72%. Benzonitrile was isolated from the mother liquor; the yield was 58%.

The diphenyl ester of the N-phosphoric acid of N'-phenylbenzamidine was cleaved similarly. The decomposition temperature was 290–300°, the yield of benzonitrile 91%, and the yield of the N-phenylamide of diphenyl phosphate 88%; the latter had m. p. 127–129°, which agrees with literature data [4].

Hydrochlorides of diphenyl esters of N-phosphoric acids of amidines of the type (I) and (II). A solution of 0.01 mole of the diphenyl ester of an N-phosphoric acid of an amidine of type (I) or (II) was saturated with dry hydrogen chloride. The mixture heated up slightly and deposited the hydrochloride as a colorless liquid. The benzene was removed in vacuum and the residual hydrochlorides were clear, thick, viscous liquids, which changed into a glassy mass on standing. The yield was quantitative. Treatment of the salts with 0.2 N alcohol solution of alkali quantitatively converted them into the starting diphenyl esters of N-phosphoric acids of amidines.

SUMMARY

The action of ammonia and amines of C-chloro-P,P-diaroxysophosphazoaroyls yielded diaryl esters of N-phosphoric acids of aromatic amidines, which had very weak basic properties and were decomposed by heating to the corresponding nitriles and amides of diphenyl phosphate.

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CONVERSIONS OF DIAZOAMINO COMPOUNDS

III. HOMOLYTIC DECOMPOSITION OF AROMATIC DIAZOAMINO COMPOUNDS

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On a number of examples it was shown that the thermal decomposition of aliphatic-aromatic triazenes has a homolytic character. The capacity of mercury in the presence of carbon tetrachloride to bind radicals with the formation of arylmercury chlorides [1] was used to demonstrate the formation of free radicals in the decomposition of diazoamino compounds. Under these conditions, 1,3-benzylphenyltriazene formed phenylmercury chloride in addition to benzylamine and benzyaniline. The decomposition of aliphatic-aromatic triazenes at 120-140° in isopropylbenzene and cyclohexene was then studied [2]. Alkylanilines, alkanes, and bicumyl and bicyclohexenyl, respectively, were isolated from the decomposition products of the triazenes. Isopropylbenzene and cyclohexene were not alkylated under these conditions. The formation of bicumyl and bicyclohexenyl is explained by dimerization of radicals formed as a result of elimination of a hydrogen atom from a solvent molecule by alkyl radicals. Rondestvedt and Blanchard [3] used 1-phenyl-3,3-dimethyltriazene

TABLE 1

Conversion of Triazenes $RNHN=NR_1 \rightleftharpoons RN=NNHR_1$

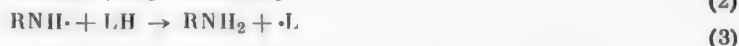
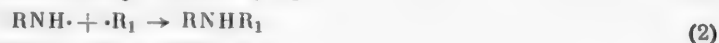
Starting triazene		Solvent or medium	Decomposition medium	Yield of conversion products (in moles per mole of triazene)		
R	R ₁			RNHR ₁	RNH ₂	R ₁ NH ₂
p-Carboxyphenyl	p-Carboxyphenyl	Anthracene	275°	0.62	0.32	—
p-Carboxyphenyl	p-Chlorophenyl	Octadecyl alcohol	275-290	0.34	(R = R ₁) 0.2 (total amines)	—
p-Carboxyphenyl	p-Tolyl	Anthracene	270-290	0.26	0.1	0.07
1'-Anthraquinonyl	p-Tolyl	Dibutyl phthalate	285-290	0.21	0.51	—
1'-Anthraquinonyl	p-Carboxyphenyl	Anthracene	280	0.52	0.33	—
2'-Anthraquinonyl	p-Tolyl	Anthracene	275	0.05	0.52	—
2'-Anthraquinonyl	p-Carboxyphenyl	Dibutyl phthalate	285-290	0.45	+*	+

* The + sign denotes that the given substances were isolated and identified, but the amounts of them were not determined.

for the arylation of toluene and isopropyl- and tert-butylbenzenes. The reaction was carried out at 100° in the presence of glacial acetic acid. The main product was found to be a mixture of ortho-, meta-, and para-isomers of the corresponding alkylbiphenyls. The arylation of the benzene homologs mentioned with benzoyl peroxide at 80-110° and N-nitrosoacetanilide at 60-80° led to analogous results. There are also other examples of the arylation of aromatic and heterocyclic compounds by aliphatic-aromatic triazenes. The decomposition of 1-phenyl-3,3-dimethyltriazene in nitrobenzene in the presence of HCl gave a 35% yield of a mixture of 2- and 4-nitrobiphenyls [4]. The role of acetic and hydrochloric acids in the decomposition of the aliphatic-aromatic triazenes has not been elucidated.

It was found that substituted diarylamines were formed during the thermal decomposition of aromatic triazenes in organic media [5, 6]. Primary aromatic amines were obtained simultaneously in considerable amounts. Table 1 shows the yield of diarylamine and primary aromatic amine from the corresponding triazene. The presence of two primary amines in decomposition products is connected with the possibility of two structures for unsymmetrical triazenes: $RNHN=NR_1$ and $RN=NNHR_1$. Aromatic diazoamino compounds were converted into diarylamines at 270-290°, when triazenes decomposed at a high rate (practically instantaneously). These conditions also differed from the above-mentioned cases of slow decomposition of aliphatic-aromatic triazenes at 100-140° in the absence of acidic agents (CH_3COOH , HCl) [3, 4] or mercury [1].

It seemed interesting to obtain evidence of the formation of free radicals during the thermal decomposition of aromatic triazenes under these conditions. As a "model" of an aromatic diazoamino compound we chose 1-p-tolyl-3-(1'-anthraquinonyl)-triazene (I), which reacts in one tautomeric form to give 1-p-tolylaminoanthraquinone (II) and 1-aminoanthraquinone (III) [6]. The decomposition of (I), proceeding with the liberation of nitrogen, could give rise to two free radicals, $RNH\cdot$ (where R = 1-anthraquinonyl) and $R_1\cdot$ (p-tolyl) (1), the interaction of which would probably form (II) (2). The formation of (III) was a secondary process, namely, the interaction of the radical $RNH\cdot$ with solvent LH (3).



To confirm the conversion scheme of triazene (I) it was necessary to isolate the products of the reaction of radical $R_1\cdot$ with the organic medium and to follow the conversions of the radicals $L\cdot$. For this purpose we studied the decomposition of (I) in anthracene, nitrobenzene, and 1,2,4-trichlorobenzene. The decomposition of (I) in anthracene at 285-290° proceeded instantaneously, but in nitrobenzene and trichlorobenzene it was complete after 1 hour. In all cases, (II) and (III) were obtained (Table 2).

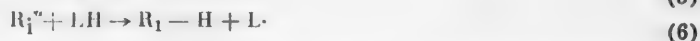
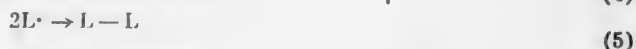
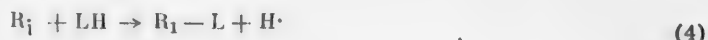
TABLE 2
Decomposition of 1-p-Tolyl-3-(1'-anthraquinonyl)-triazene in Various Solvents

Solvent, LH	Decomposition temperature	Yield of conversion products (in moles per mole of triazene)			
		1-p-tolylamino-anthraquinone, $RNHR_1$	1-aminoanthraquinone, RNH_2	unsymmetrical biaryl, R_1L	symmetrical biaryl, LL
Anthracene	285-290°	0.08	0.67	0.38	Not isolated
Nitrobenzene	211-212	0.02	0.95	0.49	—
1,2,4-Trichlorobenzene	212-213	0.04	0.91	—	0.28

In addition, 9-p-tolylanthracene (IV) was isolated when the decomposition was carried out in anthracene and 2'- and 4'-nitro-4-methylbiphenyl (V and VI) when (I) was decomposed in nitrobenzene. The formation of (IV), (V), and (VI) was evidently the result of reaction of the tolyl radical with anthracene and nitrobenzene

molecules (4). The entry of the tolyl radical into the positions ortho and para to the nitro group in the nitrobenzene molecule and the meso position of anthracene indicate the nonpolar nature of the radical.

Proof of the formation of free radicals during the thermal decomposition of (I) was also obtained by carrying out the decomposition in 1,2,4-trichlorobenzene. Instead of the expected product from the arylation of the trichlorobenzene molecule by the tolyl radical (4'-methyl-2,4,5-trichlorobiphenyl), hexachlorobiphenyl (VII) was isolated. A substance (b. p. 108-110°), corresponding to toluene in properties was obtained simultaneously. Actually, (VII) could only be formed from two equivalent trichlorophenyl residues, i.e., as a result of the dimerization of trichlorophenyl radicals (5). The formation of trichlorophenyl radicals could be the result of the abstraction of a hydrogen atom from a trichlorobenzene molecule according to Equation (3) or (6). Evidence in favor of the formation of radicals $L\cdot$ by Equation (3) is provided by the high yield of 1-aminoanthraquinone (almost quantitative in the case of trichlorobenzene and nitrobenzene).



Thus, it was possible to follow the subsequent conversions of the radicals $R_1\cdot$, arising during decomposition of triazene (I), and also of the radicals $L\cdot$, formed by secondary processes (3 and 6).

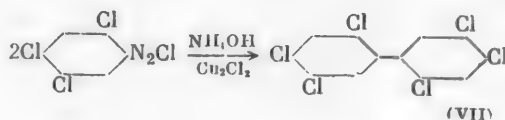
The scheme presented (1-6) illustrates only the main directions of the conversions of triazenes in organic media and does not exhaust all possible cases of reaction of the radicals with each other and with the solvent.

As a demonstration of the structure, 9-p-tolylanthracene was synthesized from 9-anthrone and p-tolylmagnesium bromide in ether under conditions differing from the synthesis of 9-phenylanthracene [7].

2'- and 4'-nitro-4-methylbiphenyls were synthesized from p-toluene diazonium chloride and nitrobenzene by the Gomberg reaction. In contrast to the conditions reported [8], the reaction was carried out at +10 to +15° instead of +5°.

2'-Nitro-4-methylbiphenyl was a yellow oil, which, on reduction and subsequent acylation, gave 2'-acetyl-amino-4-methylbiphenyl. An identical product was obtained from (V).

The hexachlorobiphenyl isolated from the products of decomposing (I) in 1,2,4-trichlorobenzene was found to be the 2,4,5,2',4',5'-isomer. 2,4,5,2',4',5'-Hexachlorobiphenyl (VII) was synthesized from 2,4,5-trichloroaniline under the conditions for the preparation of symmetrical biaryls by Vorländer's method [9]. It is known that under these conditions a carbon-carbon bond is formed by combination of the two aryl residues through the carbon atoms attached to the diazo group nitrogen. Decomposition of 2,4,5-trichlorobenzenediazonium chloride with an ammonia solution of cuprous chloride formed (VII).



EXPERIMENTAL

Decomposition of 1-p-tolyl-3-(1'-anthraquinonyl)-triazene (I)

A. In anthracene. Finely ground (I) (8 g) was introduced into anthracene (50 g), heated to 285-290°; vigorous evolution of nitrogen was observed. After 2-3 minutes the mass was cooled, ground up, and treated with methanol (1000 ml) until the filtrate was colorless. The methanol solution was concentrated to a volume of 200 ml, the light yellow crystals (anthracene with m. p. 210-211°) removed by filtration, the filtrate evaporated to dryness, and the residue dissolved in CCl_4 and chromatographed on Al_2O_3 . Three zones separated: Light yellow, violet, and dark red. The light yellow zone was eluted with CCl_4 . Removal of the solvent yielded a light yellow oil, which crystallized on standing (2.5 g). Recrystallization from alcohol yielded 1.6 g of 9-p-tolylanthracene. It formed right hexahedrons. The m. p. was 143.5-144.5°. The substance crystallized from glacial acetic acid as colorless needles with m. p. 144.5-145.5°.

Found %: C 93.65, 93.80; H 6.27, 6.00. $C_{21}H_{16}$. Calculated %: C 94.03; H 5.97.

A mixture with 9-p-tolyanthracene (m. p. 145.5-146°), obtained by synthesis, melted at 144-145°.

The violet zone was eluted with chlorobenzene. Evaporation of the solution and recrystallization of the residue from butanol yielded 1-p-tolylaminoanthraquinone. It formed ruby needles. The m. p. was 158-159°. The yield was 0.6 g. It did not depress the melting point of authentic 1-p-tolylaminoanthraquinone.

The dark red zone was eluted with ethyl acetate. 1-Aminoanthraquinone was obtained. The yield was 3.5 g and the m. p. 246-247°.

B. In nitrobenzene. A solution of 14.5 g of (I) in 120 ml of nitrobenzene was heated to 210-212° over a period of 30-45 minutes and stirred and boiled for 1 hour. The nitrobenzene was then removed in vacuum and the residue fractionally crystallized and chromatographed on Al_2O_3 . We isolated: a) 1-Aminoanthraquinone with m. p. 248-249° in a yield of 9.3 g (95%); b) 1-p-tolylaminoanthraquinone with m. p. 157-158° in a yield of 0.3 g (2%); c) a mixture of 2'- and 4'-nitro-4-methylbiphenyls in a yield of 4.6 g [0.49 mole per mole of (I)].

4'-Nitro-4-methylbiphenyl formed colorless crystals (from alcohol). The m. p. was 140-141°.

Found %: N 6.53, 6.39. $C_{13}H_{11}O_2N$. Calculated %: N 6.56.

A mixture with authentic 4'-nitro-4-methylbiphenyl (m. p. 139.5-140.5°) melted at 139-140°.

2'-Nitro-4-methylbiphenyl was a yellow oil with b. p. 146-150° (3 mm), n_D^{20} 1.6017.

Found %: N 6.91. $C_{13}H_{11}O_2N$. Calculated %: N 6.56.

Reduction with zinc dust in a mixture of acetic and hydrochloric acids and subsequent acetylation with $(CH_3CO)_2O$ yielded 2'-acetyl-amino-4-methylbiphenyl. It formed colorless needles. The m. p. was 103-104°. A mixture with the substance obtained by synthesis (m. p. 102-103°) melted at the same temperature.

C. In 1,2,4-trichlorobenzene. From the products of decomposition of (I) (14.5 g) in 1,2,4-trichlorobenzene (b. p. 212-213°), we isolated the following substances as described above: a) A colorless, oily substance (0.3 g) with b. p. 108-110° and the smell of toluene; b) 1-aminoanthraquinone with m. p. 246-247° in a yield of 8.4 g (90%); c) 1-p-tolylaminoanthraquinone with m. p. 155-156.5° in a yield of 0.6 g (4%); d) hexachlorobiphenyl as colorless needles with m. p. 137-138° in a yield of 3.6 g [0.28 mole per mole of (I)].

Found %: Cl 57.78, 57.16. $C_{12}H_4Cl_6$. Calculated %: Cl 59.0.

A mixture with 2,4,5,2',4',5'-hexachlorobiphenyl (m. p. 136.5-137.5°), obtained by synthesis, melted at 136-137°.

9-p-Tolyanthracene. From 17.2 g of p-bromotoluene and 2.8 g of magnesium turnings in 40 ml of diethyl ether we prepared a solution of p-tolylmagnesium bromide and this was stirred while a suspension of 6.9 g of 9-anthrone (m. p. 159-160°) in 35 ml of ether was added. The mixture was boiled and stirred for 2 hours, cooled to 0-5°, 40 ml of hydrochloric acid (1 : 3) added, and the mixture stirred for 1 hour. The ether layer was separated, washed with water, and steam distilled. The oily residue solidified to a colorless, crystalline mass (6 g) on cooling and this crystallized from glacial acetic acid as fine needles. The m. p. was 145.5-146°. The product was difficultly soluble in benzene, alcohol, and acetic acid in the cold, but dissolved readily on heating. The solutions had a violet fluorescence, characteristic of anthracene and its derivatives.

2,4,5,2',4',5'-Hexachlorobiphenyl. A mixture of 0.05 mole of 2,4,5-trichloroaniline and 100 ml of hydrochloric acid (2 : 1) was heated to 95-98°, rapidly cooled to +10°, NaBr added, and the suspension obtained diazotized with 20% $NaNO_2$ solution at 10-12°. After 2 hours the 1,2,4-trichlorobenzenediazonium chloride solution was filtered free from the slight precipitate and added over a period of 30 minutes at 20-25° to an ammonia solution of cuprous chloride (0.125 mole of Cu_2Cl_2 , 0.87 mole of NH_3 , and 200 ml of water). The mass was stirred for 30 minutes and then the yellow precipitate collected, washed with water, hydrochloric acid and again water, and steam distilled. The 2,4,5,2',4',5'-hexachlorobiphenyl was sublimed in vacuum. It formed colorless needles. The m. p. was 136-137°. The product formed rectangular prisms (from benzene). The m. p. was 136.5-137.5°.

2'- and 4'-nitro-4-methylbiphenyl. A solution of p-toluenediazonium chloride (obtained by diazotization of 0.5 mole of p-toluidine in 95 ml of 30% HCl with $NaNO_2$ solution) was added to a mixture of nitrobenzene

(400 ml) and a 40% solution of NaOH (155 ml) at 10-15° over a period of 3 hours and the mixture stirred for 4 hours and left to settle. The nitrobenzene layer was washed with water, hydrochloric acid, and again water. It was dried over CaCl_2 and vacuum distilled. We obtained: 1st fraction with b. p. 56-70° (2.5 mm); 2nd fraction with b. p. 160-180° (4 mm); 3rd fraction with b. p. 180-195° (4 mm). The third fraction solidified on standing. After being washed with alcohol, it consisted of colorless crystals (2 g) with m. p. 138.5-139.5°. Cooling the second fraction to 0° yielded a further 1.8 g of 4'-nitro-4-methylbiphenyl with m. p. 138-139.5°. The total yield was 3.8 g (4%). The product formed polyhedra (from alcohol). The m. p. was 139.5-140.5°. The oil remaining from the second fraction was vacuum distilled. The yield of 2'-nitro-4-methylbiphenyl was 12 g (11%). The b. p. was 146-150° (3 mm).

2'-Acetylamino-4-methylbiphenyl. 2'-Nitro-4-methylbiphenyl (3 g) was dissolved in glacial acetic acid (30 ml), concentrated HCl (30 ml) and ice (30 g) added, and 12 g of zinc dust gradually introduced; at the end of the reduction the temperature of the mass was 15-20°. The filtered solution was neutralized with NaOH, the liberated oil extracted with ether and dried with CaCl_2 , and the ether removed. The yellow-brown residue was dissolved in 10 ml of glacial acetic acid, heated to 40°, 10 ml of acetic anhydride added dropwise, and the mixture stirred at 95° for 2 hours. At the end of the acylation, the acetic acid and anhydride were removed in vacuum and the residue recrystallized from alcohol. The yield was 1 g. The product formed colorless needles. The m. p. was 102-103°.

Found %: N 6.20, 6.22. $\text{C}_{15}\text{H}_{15}\text{ON}$. Calculated %: N 6.22.

SUMMARY

1. A study was made of the products from thermal decomposition of 1-p-tolyl-3-(1'-anthraquinonyl)-triazene in anthracene, nitrobenzene, and 1,2,4-trichlorobenzene. In addition to 1-p-tolylaminoanthraquinone and 1-aminoanthraquinone, we isolated 9-p-tolylanthracene, 2'- and 4'-nitro-4-methylbiphenyl, and 2,4,5,2',4',5'-hexachlorobiphenyl, whose formation indicated the homolytic nature of the decomposition of the aromatic triazene.

2. A scheme was proposed explaining the conversions of the triazene in organic media, proceeding by a free radical mechanism.

3. 9-p-Tolylanthracene and 2,4,5,2',4',5'-hexachlorobiphenyl were prepared and characterized for the first time.

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*Original Russian pagination. See C. B. Translation.

**See C. B. Translation.

ADDITION OF NITROALKANES TO DIBENZALACETONE

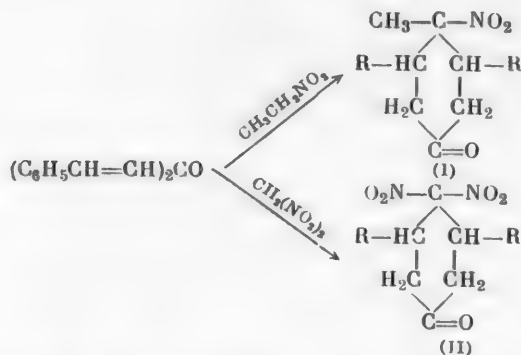
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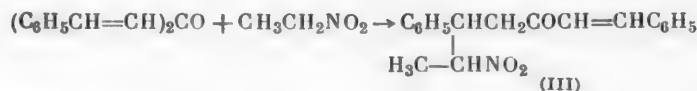
The reaction of dibenzalacetone with nitroalkanes was first described in 1924 by Kohler [1]. The author was able to add nitromethane to dibenzalacetone in the presence of sodium methylate to form 4-nitro-3,5-diphenylcyclohexanone [2]. Since then, reactions between dibenzalacetone and compounds with a labile hydrogen atom have been mentioned in several papers [3, 4].

In previous work we studied the addition of nitroalkanes to benzalacetone [5]. The present work was aimed at determining how the reaction of dibenzalacetone with nitroalkanes proceeds in relation to the number of nitro groups and the number of labile hydrogen atoms. It might be assumed that the addition to dibenzalacetone proceeds stepwise and that the final product formed depends on the ratio of the reactants.

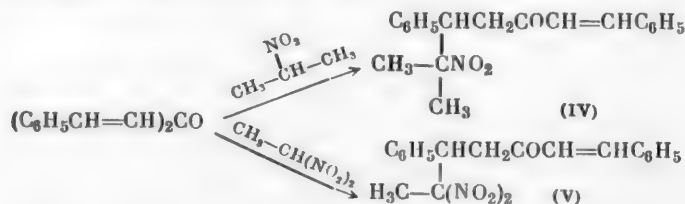
The addition of nitroethane and dinitroethane to dibenzalacetone in the ratio of 5 : 1 in the presence of catalyst led to the formation of cyclic products (I) and (II).



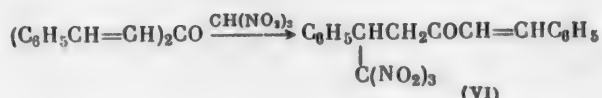
Reaction of dibenzalacetone and dinitromethane in equimolecular amounts led to the formation of product (II). Reaction of dibenzalacetone and nitroethane in equimolecular amounts under analogous conditions led to the formation of product (III).



2-Nitropropane and 1,1-dinitroethane added to dibenzalacetone with a ratio of 5 : 1 and the same catalyst to form 2-nitro-2-methyl-3,7-diphenylhepten-6-one-5 (IV) and 2,2-dinitro-3,7-diphenylhepten-6-one-5 (V).



Trinitromethane added to dibenzalacetone without catalyst with the formation of 1,1,1-trinitro-2,6-diphenylhexen-5-one-4 (VI).



Nitroalkane	Reagent ratio	Reaction time (in hours)	Substance obtained	Melting point	
				ketone	dinitrophenyl-hydrazone
Dinitromethane	1 : 1	24	(I)	131.5°	202°
Nitroethane	5 : 1	10	(II)	188	221.5
Nitroethane	1 : 1	—	(III)	159	220
2-Nitropropane	1 : 2	12	(IV)	205	216
1,1-Dinitroethane	2.5 : 1	50	(V)	130.5	185
Trinitromethane	2 : 1	12	(VI)	96	157.5

EXPERIMENTAL

Dibenzalacetone was prepared from acetone and benzaldehyde and had m. p. 111-112°. Literature data [5]: m. p. 112°

Nitroalkanes were added to dibenzalacetone in the presence of an alcohol solution of trimethylphenyl-ammonium ethoxide at 75-85°. The reaction conditions and the properties of the ketones obtained are given in the table.

4,4-Dinitro-3,5-diphenylcyclohexanone-1 (I). From 5 g of dibenzalacetone and 2.1 g of dinitromethane in an ethanol medium we obtained 1.02 g (15%) of (I).

Found %: C 63.72; 63.54; H 4.85, 4.83; N 7.59, 7.55. $C_{18}H_{16}O_5N_2$. Calculated %: C 63.50; H 4.71; N 8.26.

4-Nitro-4-methyl-3,5-diphenylcyclohexanone (II). From 3.7 g of nitroethane and 4 g of dibenzalacetone in 15 g of ethanol we obtained 2.6 g (40%) of (II).

Found %: C 73.87, 73.85; H 6.24, 6.36; N 4.59, 4.73. $C_{19}H_{19}O_3N$. Calculated %: C 73.58; H 6.15; N 4.52.

1-Nitro-1-methyl-2,6-diphenylhexen-5-one-4 (III). From 2.25 g of nitroethane and 6.7 g of dibenzalacetone in 20 ml of alcohol we obtained 4 g (45%) of (III).

Found %: C 73.64, 73.89; H 6.42, 6.24; N 4.83, 4.60. $C_{19}H_{17}O_3N$. Calculated %: C 74.42; H 6.20; N 4.55.

2-Methyl-2-nitro-3,7-diphenylhepten-6-one-5 (IV). From 8.9 g of 2-nitropropane and 5 g of dibenzalacetone in 15 ml of alcohol we obtained 2 g (30%) of product.

Found %: C 73.80, 73.90; H 6.47, 6.40; N 4.84. $C_{20}H_{21}O_3N$. Calculated %: C 74.30; H 6.50; N 4.34.

2,2-Dinitro-3,7-diphenylhepten-6-one-5 (V). From 6.75 g of 1,1-dinitroethane and 7 g of dibenzalacetone in 20 ml of alcohol we obtained 1 g (45%) of (V).

Found %: C 64.35, 64.43; H 5.10, 5.09; N 7.90, 7.80. $C_{18}H_{15}O_5N_2$. Calculated %: C 64.40; H 5.09; N 7.90.

1,1,1-Trinitro-2,6-diphenylhexen-5-one-4 (VI). From 9 g of trinitromethane in 25 ml of alcohol and 7 g of dibenzalacetone we obtained 8.7 g (78%) of (VI).

Found %: C 55.60, 55.85; H 3.80, 3.93; N 10.22, 10.14. $C_{18}H_{25}O_7N_3$. Calculated %: C 56.10; H 3.90; N 10.90.

SUMMARY

From experimental data obtained it was established that the addition of nitroalkanes containing one labile hydrogen atom to dibenzalacetone under the conditions studied occurs only at one double bond. If the nitroalkane contains two labile hydrogen atoms a cyclic product is formed due to the two double bonds of dibenzalacetone. However, in this case the addition depends strongly on the acidity of the starting nitroalkane.

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REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

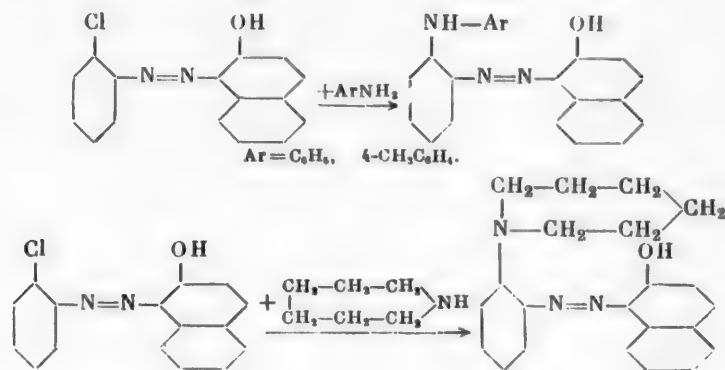
VIII. REACTION OF 2-CHLOROBENZENEAZO-2'-NAPHTHOL WITH AMINES

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The possibility of replacing halogen in azo dyes by alkyl- and arylamino groups has been reported only in the patent of Delfs [1], according to which the reaction of monoazo dyes from o-chlorometanilic acid and 2-naphthol in the presence of copper compounds with piperidine in an aqueous medium, with aniline in aqueous pyridine, and with excess ethanolamine leads to replacement of the chlorine atom by the corresponding nitrogen-containing residue. No examples with dyes which did not contain sulfonic groups and were insoluble in aqueous media were given in Delfs' patent.

We reacted 2-chlorobenzeneazo-2'-naphthol (azo dye from 2-chloroaniline and 2-naphthol) with aniline, p-toluidine, and hexamethyleneimine in the presence of copper sulfate and sodium carbonate in an aqueous medium at 95° and in all cases established that the corresponding chlorine-free aryl- and alkylaminoazo dyes were formed as the copper complexes. It was found that



the reaction with hexamethyleneimine proceeded more rapidly and the copper complex of the substituted dye was decomposed to the copper-free dye more readily than in the case of reactions with aromatic amines. This was probably connected with the difference in basicity of the amines.

In experiments on the reaction of halogen-containing azo dyes with alcohols, it was shown [2, 3] that replacement of the halogen atom by an alkoxy group proceeds smoothly in the absence of free copper salt if the starting dye itself is introduced into the reaction as its copper complex. We reacted the copper complex of 2-chlorobenzeneazo-2'-naphthol with aniline and also observed that a dye was formed with a phenylamino group instead of the chlorine atom. Thus, it is possible that replacement of halogen in o-halo-o'-hydroxyazo dyes by nitrogen-containing residues in the presence of copper salts occurs in the intermediately formed copper complex of the starting dye.

EXPERIMENTAL

Replacement of chlorine by arylamino groups. A sample of 2.8 g of the starting azo dye from 2-chloroaniline and 2-naphthol (m. p. 167° [4]) was dissolved in 20 ml of pyridine at 70°, then 60 ml of water added and to the fine suspension obtained were added solutions of 2 g of calcined soda in 10 ml of water and 2.5 g of copper sulfate in 10 ml of water. Then either 1.9 g of aniline or 2.2 g of p-toluidine was added. The mixture formed was heated and stirred for 8 hours at 95°. The cooled reaction mixture was diluted with an equal volume of water and the precipitate collected and washed with dilute hydrochloric acid to remove pyridine and excess aromatic amine. The black (appreciable bronze luster in the case of aniline or with a greenish tinge in the case of p-toluidine) precipitate of the copper complex of the substituted dye was heated under reflux for 5 hours with 20% hydrochloric acid to decompose the complex and then the free dye was collected, washed with water to remove chlorine ions, and dried at room temperature. A test for chlorine was negative.

We obtained 2.75 g (81.8%) of the phenylamino substituted dye. After recrystallization from a mixture of glacial acetic acid and alcohol (1 : 1) it formed fine red needles with m. p. 245°. The dye was soluble in benzene, toluene, chlorobenzene, dioxane, carbon tetrachloride, and dichloroethane, less soluble in glacial acetic acid methyl and ethyl alcohols, acetone, and ligroine, and insoluble in water. A solution in concentrated sulfuric acid had a crimson color.

Found %: N 12.36. $C_{22}H_{17}ON_3$. Calculated %: N 12.38.

We obtained 2.7 g (77.7%) of 4-methylphenylamino-(p-tolylamino-) substituted dye. After recrystallization from a mixture of benzene and alcohol (1 : 2) it formed long, bright red needles with m. p. 237°. The dye was soluble in benzene, toluene, chlorobenzene, and acetone, difficultly soluble in glacial acetic acid and methyl and ethyl alcohols, and insoluble in water. The solution in concentrated sulfuric acid had a violet color.

Found %: N 11.48. $C_{23}H_{19}ON_3$. Calculated %: N 11.89.

Reaction of copper complex of 2-chlorobenzeneazo-2'-naphthol with aniline. A sample of 0.5 g of the copper complex of the starting dye (m. p. 252-253° [2]) was dissolved in 3 ml of pyridine at 70° and then 10 ml of water was added, and to the suspension obtained were added a solution of 0.32 g of calcined soda in 2 ml of water and 0.3 g of aniline. The mixture was heated for 8 hours at 95° and then diluted with water; the precipitate was collected, washed free from pyridine and aniline with dilute hydrochloric acid, and heated under reflux for 6 hours with 20% hydrochloric acid to decompose the copper complex. The dye was then collected, washed with water to remove chlorine ions, and dried at room temperature. A test for chlorine was negative. The yield was 0.3 g (65.2%); after recrystallization from a mixture of glacial acetic acid and alcohol (1 : 1), the substance had m. p. 244-245°. A mixed melting point with the phenylamino substituted dye was not depressed.

Replacement of chlorine by the hexamethyleneimine group. A sample of 2.8 g of the starting dye was dissolved in 20 ml of pyridine at 70°, then 45 ml of water was introduced and to the suspension formed were added solutions of 2.5 g of copper sulfate in 5 ml of water and 6.25 g of potassium sodium tartrate in 5 ml of water. Then 6.4 g of hexamethyleneimine (19.4 g of a 33% solution) was added, the mixture heated to 95°, and a solution of 1.4 g of sodium hydroxide in 13 ml of water added over a period of 30 minutes. The mixture was heated with stirring for 5 hours at 95°, then cooled and diluted with an equal volume of water; the precipitate was collected and heated under reflux for 10-15 minutes with 20% hydrochloric acid to decompose the copper complex. The hexamethyleneimino substituted dye was collected, washed free from chlorine ions, and dried at room temperature. A test for chlorine was negative. The yield was 2.5 g (73.5%); after recrystallization from benzene, the substance formed flat, reddish orange needles with m. p. 241-242°. They were readily soluble in the cold in dioxane and chlorobenzene, sparingly soluble in benzene, toluene, acetone, and carbon tetrachloride, and insoluble in glacial acetic acid and methyl and ethyl alcohols; on heating they dissolved readily in benzene and toluene, less so in carbon tetrachloride, glacial acetic acid, and acetone, and sparingly in methyl and ethyl alcohols. They were insoluble in water and ligroine.

Found %: N 12.00. $C_{22}H_{23}ON_3$. Calculated %: N 12.16.

SUMMARY

1. By reaction of the azo dye from 2-chloroaniline and 2-naphthol with aniline, p-toluidine, and hexamethyleneimine in a water-pyridine medium in the presence of copper sulfate under mild conditions (at 95°) the chlorine atom was replaced by the corresponding aryl- and alkylamino groups.

2. It was found that the chlorine atom was replaced by the phenylamino group by reaction of the copper complex of the azo dye from 2-chloroaniline and 2-naphthol with aniline in the absence of free copper salt.

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COPOLYMERIZATION OF POLY-1,3-BUTYLENE GLYCOL FUMARATE WITH ALLYL ESTERS OF ACIDS OF PHOSPHORUS*

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The reaction of unsaturated polyesters with vinyl monomers forms cross-linked copolymers which are used as binding materials in the production of reinforced plastics. It seemed interesting to study the copolymerization of unsaturated derivatives of acids of phosphorus with polyglycol fumarates as the introduction of phosphorus into a polymer molecule raises fire-resistance, heat-resistance and resistance to wear and action of aggressive agents. These properties are of great importance in improving the quality of reinforced plastics.

In the present work we investigated the copolymerization of poly-1,3-butylene glycol fumarate with allyl diethylphosphonoacetate and allyl ethyl phosphite.

As characteristics of the relative activities of these compounds in copolymerization with polyesters we determined the copolymerization constants of the systems: 1) Poly-1,3-butylene glycol fumarate-allyl diethylphosphonoacetate, $r_1 = 10.0 \pm 2.0$, $r_2 = 0.075 \pm 0.075$; 2) poly-1,3-butylene glycol fumarate-allyl ethyl phosphite, $r_1 = 5.5 \pm 2.5$, $r_2 = 0.035 \pm 0.035$. The values of the copolymerization constants of the systems investigated show that allyl derivatives of acids of phosphorus have low activity in copolymerization with unsaturated polyesters. Fumaric units of the polyester reacted considerably more actively with their own radical and with the

radical of the allyl derivatives of phosphorus acids. The position of the allyl bond in the esters investigated had hardly any effect on their activity. This behavior of allyl derivatives of phosphorus acids is in accord with the behavior of allyl derivatives of other classes of compounds. Thus, in the copolymerization of maleic anhydride with allyl acetate the latter reacted very weakly with its own radical, though the maleic anhydride radical reacted more actively with allyl acetate than with its own monomer. In the copolymerization of styrene with allyl acetate and allyl chloride, the styrene reacted much more actively with the allyl derivatives [1].

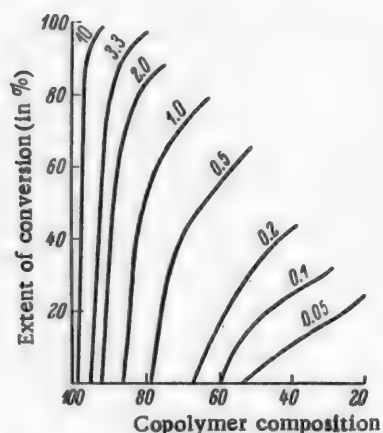


Fig. 1. Integral composition diagram of copolymers of poly-1,3-butylene glycol fumarate and allyl diethylphosphonoacetate. The figures on the curves show the polyester content in moles per mole of monomer.

From the copolymerization constants obtained we calculated the integral composition of the copolymers. The composition diagrams for the systems investigated had the same character and therefore we only give the diagram for the system poly-1,3-butylene glycol fumarate-allyl diethylphosphonoacetate. The diagram shows that the composition of the copolymers approached an azeotrope only in the region of very low polyester concentrations (at a polyester to monomer ratio of 10 : 1) (Fig. 1). At ratios close to the azeotrope, the copolymers were clear, solid, incombustible, glassy products.

* Communication 7 of a series of works on the copolymerization of unsaturated polyesters with vinyl and allyl monomers.

The change in the heat-resistance of the copolymers in relation to the starting ratios of the compounds was investigated by the thermomechanical method [2]. Figures 2 and 3 show thermomechanical curves for the copolymers of the polyester and allyl diethylphosphonoacetate at various ratios of the starting components. The

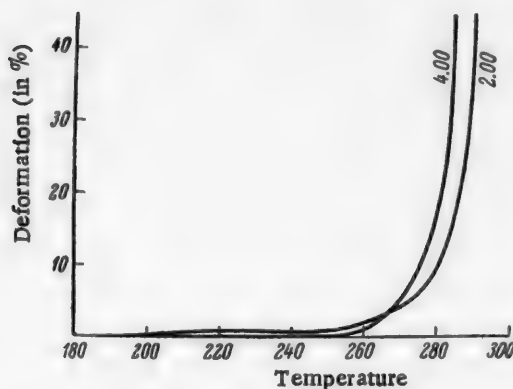


Fig. 2. Thermomechanical curves for the system poly-1,3-butylene glycol fumarate-allyl diethylphosphonoacetate. The figures on the curves show the polyester content of the starting mixture in moles per mole of vinyl acetate.

study of the copolymer deformation in relation to temperature showed that the closer the component ratio was to the azeotrope, the higher was the temperature at which deformation began. The fall in the temperature of the beginning of deformation for nonazeotropic copolymers was evidently caused by their inhomogeneity. On comparing the thermomechanical curves, attention is attracted by the fact that at ratios close to the azeotrope, the temperature of the beginning of decomposition was lower for the allyl derivative in which the allyl was bound to phosphorus through oxygen (200-210°). If the allyl was bound to the phosphorus through the acetic acid residue, the temperature of the beginning of decomposition was higher (270-280°).

EXPERIMENTAL

Poly-1,3-butylene glycol fumarate was obtained by polycondensation of equimolecular amounts of maleic anhydride and 1,3-butylene glycol in a stream of nitrogen. The polyester obtained had an acid number of 34.66.

Allyl diethylphosphonoacetate was obtained by the Arbuzov

rearrangement [3]. Allyl ethyl phosphite was obtained by heating diethyl phosphite with allyl alcohol in the presence of phosphoric acid [4].

Copolymerization of esters of phosphorus acids with poly-1,3-butylene glycol fumarate. The copolymerization was carried out in a nitrogen atmosphere in sealed ampoules at $80 \pm 0.1^\circ$ and at various ratios of polyester and monomer. After definite time intervals the ampoules were opened and the contents treated with acetone.

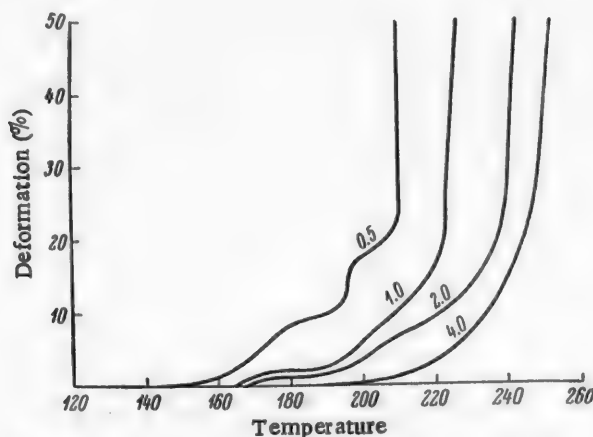


Fig. 3. Thermomechanical curves for the system poly-1,3-butylene glycol fumarate-allyl ethyl phosphite. The figures on the curves show the polyester content in moles per mole of monomer.

The copolymer was washed by decantation with acetone for 4-5 days until the polyester was completely removed (the addition of water to the acetone did not give turbidity). The washed copolymers were dried in a vacuum drying oven at 80° to constant weight. The dried copolymers were pressed into tablets at a pressure of

150 kg/cm² and 200°. The tablets were powdered and the density of the copolymers determined pycnometrically. The phosphorus content was determined by Nelman's method [5].

Determination of copolymerization constants. The constants for the systems poly-1,3-butylene glycol fumarate—esters of phosphorus acids were determined by means of the integral equation of Mayo and Lewis [6] with the introduction of a correction for the unreacted polyester units.

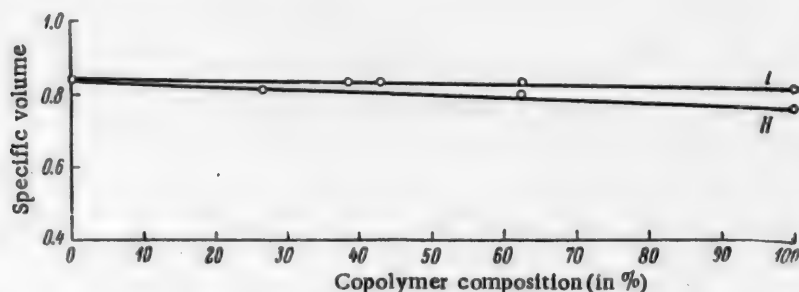


Fig. 4. Graph for determining the specific volume of polymers of allyl esters of phosphorus acids. I) Allyl phosphite—vinyl acetate ($\delta = 0.8100$), II) allyl diethylphosphonoacetate—vinyl acetate ($\delta = 0.7650$).

The number of unreacted polyester units was determined by a method based on the rule of additivity of specific volumes and the definite value of the shrinkage of monomers during polymerization [7].

The number of double bonds was determined by the formula

$$x = \frac{a \cdot \delta_p + b \cdot \delta_M - \delta_C}{P},$$

where x is the weight fraction of reacted polyester units in the copolymer; a and b are the weight fractions of monomer and polyester in the copolymer, δ_p , δ_M , and δ_C are the specific volumes of the polyester polymer, the monomer polymer, and the copolymer, and P is the specific shrinkage of a polyester unit.

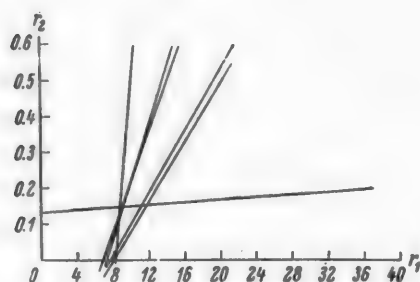


Fig. 5. Graphical determination of the copolymerization constants for the system poly-1,3-butylene glycol fumarate—allyl ethyl phosphite.

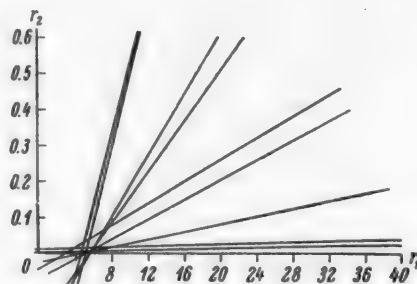


Fig. 6. Graphical determination of the copolymerization constants for the system poly-1,3-butylene glycol fumarate—allyl ethyl phosphite.

The specific shrinkage of a polyester unit was determined from a comparison of the specific volumes of the copolymer of diethyl fumarate and styrene [7]. The specific shrinkage for a unit of poly-1,3-butylene glycol fumarate equaled 0.0971.

The specific volume of polymers of allyl esters of phosphorus acids was determined graphically on the basis of the additivity of the specific volumes of their copolymers with vinyl acetate.

Copolymerization of esters with vinyl acetate was carried out in a nitrogen atmosphere in sealed ampoules at various component ratios. After the reaction mixture had been cooled it was dissolved in chloroform and the copolymer precipitated with ligroline, washed, and dried in a vacuum drying oven at 80°. The density of the copolymers was determined and they were analyzed for phosphorus.

Figure 4 shows the graphical determination of the specific volume of polymers of allyl esters of phosphorus acids. The specific volume of the polymer of allyl diethylphosphonoacetate was 0.8100 and that of the allyl ethyl phosphite polymer, 0.7650.

Figures 5 and 6 give the graphical calculation of the copolymerization constants of poly-1,3-butylene glycol fumarate with allyl esters of phosphorus acids.

The integral composition diagrams were calculated from the equation of Gindin, Abkin, and Medvedev [8] with allowance for the change in composition of the reaction mixture during the process [9].

The thermomechanical investigation of the copolymers was made on the apparatus constructed by Tseitlin, Gavrilov, Velikovskaya, and Kochkin [10]. The load acting on the sample equaled 40 kg/cm². Copolymers for thermomechanical testing were obtained by block polymerization of poly-1,3-butylene glycol fumarate with allyl esters of phosphorus acids in ampoules in the presence of 1% benzoyl peroxide for 16 hours at 80°. Samples 8 mm in diameter and 3 mm thick were cut from the blocks.

SUMMARY

1. The copolymerization of poly-1,3-butylene glycol fumarate with allyl derivatives of phosphorus acids was investigated. The copolymerization constants of the systems poly-1,3-butylene glycol fumarate-allyl phosphonoacetate and poly-1,3-butylene glycol fumarate-allyl ethyl phosphite were determined.
2. It was shown that allyl esters of phosphorus acids have a lower activity than fumaric links of the polyester in copolymerization with unsaturated polyesters.
3. It was shown that the position of the allyl bond relative to the phosphorus atom in the cases investigated did not affect the activity of allyl esters of phosphorus acids in their copolymerization with polyesters.
4. The results of thermomechanical investigation of the copolymers of allyl esters of phosphorus acids and poly-1,3-butylene glycol fumarate show that deformation of copolymers with non-azeotropic ratios begins at a lower temperature than for copolymers with ratios close to the azeotropic value.

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ORGANOBORON COMPOUNDS

LI. • SYNTHESIS OF ALKYLBORON DIFLUORIDES FROM TRIALKYLBORONS AND BORON TRIFLUORIDE ETHERATE

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The first representative of alkylboron difluorides, methylboron difluoride, was obtained by the action of boron trifluoride on methylboric anhydride [1]. It was subsequently shown that the reaction between boron trifluoride and alkylboric anhydrides is a general method of synthesizing alkylboron difluorides [2]. n-Butylboron difluoride may also be obtained by the action of boron trifluoride on n-butylboric ester [3]. It was reported that ethylboron difluoride was formed by the action of diborane on tetrafluoroethylene [4]. Buis, Davis, and Thomas [5] recently showed that heating (200°) a mixture of tri-n-butylboron and boron trifluoride, in a ratio of 1 : 2, in an autoclave gave a 90% yield of n-butylboron difluoride.

Our investigation showed that alkylboron difluorides may be obtained by the addition of boron trifluoride etherate to trialkylborons, heated to 200-220°; this process does not require the use of an autoclave. For complete conversion it was necessary to fit the reaction flask with a column to prevent removal of the boron trifluoride etherate from the reaction sphere and to introduce the etherate (from a dropping funnel extending to the bottom of the flask) at such a rate that the temperature of the liquid distilling (a mixture of ether and alkylboron difluoride) was not more than 2-3° above the boiling point of the alkylboron difluoride formed.

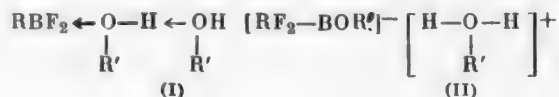
By this method we were able to obtain isoamylboron and n-hexylboron difluorides in a pure state in yields of 77-85%.



From tri-n-butylboron we obtained n-butylboron difluoride as a mixture with diethyl ether. It was impossible to separate this mixture by fractional distillation as ether and the difluoride have similar boiling points. n-Butylboron difluoride was isolated as the complex with isobutylamine.

The chemical properties of alkylboron difluorides have been investigated very little. There is a report that n-butylboron difluoride does not react with alcohols, but reacts with a mixture of alcohol and alkylboron dichloride to form n-butylfluoboric ester [5].

However, we established that alkylboron difluorides are not inert toward alcohols and form complex compounds with them in a ratio of 1 : 2, which can be vacuum distilled. We prepared compounds of isoamylboron difluoride with methyl and n-butyl alcohols and of n-hexylboron difluoride with n-butyl alcohol with the composition $RBF_2 \cdot 2R'OH$. As Meerwein found [6], boron trifluoride forms analogous trimolecular complexes with alcohols. The complex compounds of alkylboron difluorides with alcohols may have the structure (I) or (II).



* For communication XLVII see Doklady Akad. Nauk SSSR, 127, 1023 (1959), XLVIII-L, see Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 1862, 1867, and 1869 (1959). (Original Russian pagination, see C. B. translations).

Since the complexes can be distilled, structure (I) is more probable than the heteropolar structure (II).

Alkylboron difluorides react with tertiary amines to form molecular compounds in a ratio of 1 : 1 and the complexes of ethylboron difluoride with triethylamine [4] and of n-butylboron difluoride with pyridine [7] have been described.

Alkylboron difluorides also form complex compounds with the composition $\text{RBF}_2 \cdot \text{R}'\text{NH}_2$ with primary amines, but do not undergo an exchange reaction with them as might have been expected in analogy with alkylboron dichlorides [8]. We prepared n-hexyldifluoroethylaminoboron and n-butyldifluoroisobutylaminoboron.

EXPERIMENTAL

All operations with organoboron compounds were carried out in a nitrogen atmosphere.

Isoamylboron difluoride. Into a two-necked flask fitted with a dropping funnel extending to the bottom and a column, attached to a distillation condenser was placed 58.6 g of triisoamylboron. The triisoamylboron was heated to 200–210° (temperature of metal bath) and over a period of 6.5 hours, 70.5 g of boron trifluoride etherate was added at such a rate that the temperature of the liquid distilling did not exceed 60°. At the end of the reaction, the products collected in the receiver were distilled on a column with an efficiency of 20 theoretical plates. We obtained 69.6 g of a substance with b. p. 57–59°, which was isobutylboron difluoride (77% yield) and which had b. p. 58° and d_4^{20} 0.9567.

Found %: C 50.99, 51.03; H 9.86, 9.68. $\text{C}_6\text{H}_{11}\text{BF}_2$. Calculated %: C 50.06; H 9.24.

n-Hexylboron difluoride. The experiment was analogous to the previous one. To 31.9 g of tri-n-hexylboron, heated to 200–215°, was added 33.6 g of boron trifluoride etherate over a period of 5 hours at such a rate that the boiling point of the liquid distilling did not rise above 95°. The reaction products were distilled on a column with an efficiency of about 20 theoretical plates. We obtained 40.8 g of n-hexylboron difluoride with b. p. 89–90° (according to literature [2]; B. p. 91.9–92°). The yield was 85%.

Ether solution of n-butylboron difluoride. The experiment was analogous to the previous one. To 26.6 g of tri-n-butylboron at 200–220° was added 41 g of boron trifluoride etherate over a period of 5 hours; the boiling point of the liquid distilling was 38–45°. Subsequent distillation of the reaction products yielded a fraction with b. p. 39–40° (yield 49.2 g), which was a solution of n-butylboron difluoride in ether.

Found %: B 5.90, 5.41; F 22.45, 22.26.

Calculation showed that the solution contained 28 g of n-butylboron difluoride.

Complex compound of isoamylboron difluoride with methyl alcohol. To 8.4 g of isoamylboron difluoride contained in a three-necked flask with a dropping funnel, a nitrogen lead, and a reflux condenser, was added 4.1 g of methyl alcohol over a period of 15 minutes; heat evolution was observed. After 30 minutes, the mixture was vacuum distilled. We obtained a fraction with b. p. 34–37° (30 mm), which was the complex compound of isoamylboron difluoride with two molecules of alcohol. The yield was 8.0 g (67%); d_4^{20} 0.9473; n_D^{20} 1.3825.

Found %: C 44.97, 45.29; H 10.10, 10.33; B 6.08, 6.28; F 20.43, 20.96. $\text{C}_7\text{H}_{19}\text{O}_2\text{BF}_2$. Calculated %: C 45.68; H 10.41; B 5.88; F 20.65.

Complex compound of isoamylboron difluoride with n-butyl alcohol. Over a period of 10 minutes, 6.1 g of n-butyl alcohol was added to 55.5 g of isoamylboron difluoride when the mixture evolved heat. Subsequent distillation gave 9.3 g of a fraction with b. p. 43–47° (10 mm), which was the complex compound of isoamylboron difluoride with two molecules of n-butyl alcohol. The yield was 87%; d_4^{20} 0.8891, 1.4050.

Found %: C 58.88, 58.93; H 11.40, 11.57; B 4.50, 4.12; F 14.66, 13.97. $\text{C}_{13}\text{H}_{31}\text{O}_2\text{BF}_2$. Calculated %: C 58.21; H 11.65; B 4.03; F 14.17.

Found %: C 60.04, 59.98; H 12.26, 12.53; B 4.10, 4.31; F 12.95, 12.95. $\text{C}_{14}\text{H}_{33}\text{O}_2\text{BF}_2$
Calculated %: C 59.58; H 11.73; B 3.83; F 13.46.

Complex compound of n-hexylboron difluoride with n-butyl alcohol. Analogously, from 7.3 g of n-hexylboron difluoride and 6.9 g of n-butyl alcohol we obtained 11 g (85%) of the complex compound of n-hexylboron difluoride with two molecules of n-butyl alcohol; it had b. p. 47–50° (9mm) and d_4^{20} 0.8901.

n-Hexyldifluoroethylaminoboron. To a solution of 6.9 g of ethylamine in 10 ml of absolute ether, cooled to -70° in a three-necked flask with a nitrogen inlet, a dropping funnel, and an outlet tube, was added 6.7 g of n-hexylboron difluoride, diluted with 5 ml of absolute ether. A white, crystalline precipitate formed immediately and this dissolved when the temperature was raised to room temperature. The solvent and unreacted starting materials were removed from the reaction mixture in the vacuum of a water pump. The white crystalline residue was the product of the addition of ethylamine to n-hexylboron difluoride. We obtained 6.7 g of substance (75%). After two recrystallizations from ether, the complex had m. p. $112-114^{\circ}$.

Found %: C 53.47, 53.49; H 11.58, 11.55; B 5.48, 5.88; F 22.38, 21.98; N 7.46, 7.58. $C_8H_{20}NBF_2$.
Calculated %: C 53.65; H 11.26; B 6.04; F 21.22; N 7.82.

n-Butyldifluoroisobutylaminoboron. To 6.3 g of ether solution of n-butylboron difluoride was added 4.4 g of isobutylamine, diluted with 5 ml of absolute ether. Removal of the solvent and unreacted starting materials in vacuum yielded 6.3 g of a white crystalline substance, which was a complex compound of n-butylboron difluoride with isobutylamine; it had m. p. $44-50^{\circ}$.

Found %: C 52.65, 52.61; H 10.93, 11.23; B 6.78, 6.79; N 7.78, 7.42. $C_8H_{20}NBF_2$. Calculated %: C 53.65; H 11.26; B 6.04; N 7.82.

SUMMARY

1. Trialkylborons react with boron trifluoride etherate at $200-215^{\circ}$ to form alkylboron difluorides.
2. Alkylboron difluorides react with alcohols to form complex compounds with the composition $RBF_2 \cdot 2R'OH$.
3. With primary amines, alkylboron difluorides give complex compounds with the compositions $RBF_2 \cdot R'NH_2$.

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ISOXAZOLE COMPOUNDS

I. SOME REACTIONS OF 3-METHYL-4-BENZOYL-5-CHLOROISOXAZOLE

I. Ya. Postovskii and S. V. Sokolov

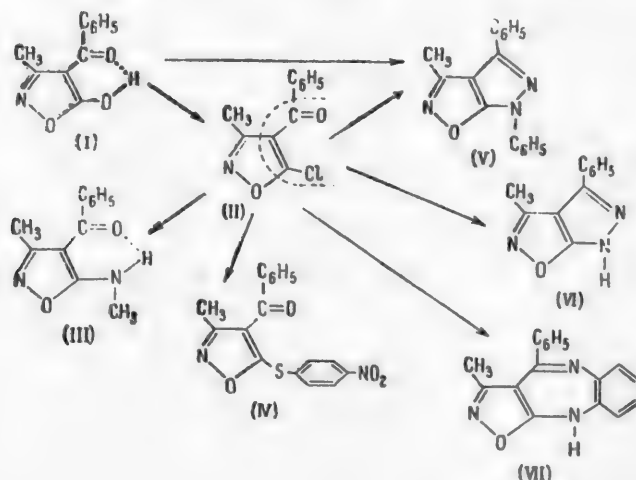
Ural Polytechnic Institute

In connection with the discovery of the isoxazole antibiotic cycloserine, the chemistry of isoxazole has acquired considerable interest. Intending to synthesize a series of new amines and other compounds of isoxazole in connection with this, we turned our attention to the work [1], in which it was shown that the reaction of 3-methyl-4-benzoyl-5-hydroxyisoxazole (I) with thionyl chloride formed chloride (II), which has a high reactivity. We reacted this chloride with methylamine and also with the sodium salt of p-nitrothiophenol and readily obtained the methylamino derivative (III) in the first case and the expected sulfide (IV) in the second, which confirms the presence of a labile chlorine atom in compound (II).

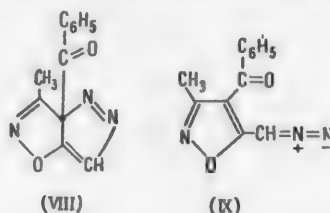
However, chloride (II) was interesting not only because it contained a reactive chlorine atom, but also because it contained a β -chlorovinyl ketone grouping, the vinyl bond of which was part of the heterocyclic ring (this grouping is shown by a dotted line in the formula). Many syntheses of heterocyclic compounds have recently been achieved by use of β -chlorovinyl ketones [2-4].

In this connection it seemed interesting to carry out reactions with the chloroisoxazole (II) to prepare isoxazoles, condensed with a second heterocycle. Chloride (II) was reacted with phenylhydrazine and hydrazine hydrate to form pyrazolooisoxazoles (V) and (VI), which have not been described previously in the literature. Compound (V) was also obtained by reaction of 5-hydroxyisoxazole (I) with phenylhydrazine, which demonstrates the position of the phenyl on the nitrogen in compound (V). Thus, the reaction proceeded unequivocally, giving only one of the possible isomers as in the cases presented in [2].

Reaction of the chloride with o-phenylenediamine gave a quantitative yield of a compound, which according to analysis results was evidently a tricyclic compound, the diazacycloheptatriene (VII).



In analogy with the reaction of diazomethane with a β -chlorovinyl ketone, which forms a 3-acylpyrazole hydrochloride [3], we reacted chloride (II) with diazomethane. This yielded a stable, readily crystallizable, yellow product, whose elementary composition corresponded to that of the expected double heterocycle (VIII).



It seemed strange that the product was not liberated from an ether solution in the form of a hydrochloride, but was obtained as a substance which did not have basic properties. In this connection the idea arose that the compound obtained might have been the unclosed diazomethene of structure (IX).

This hypothesis was supported by the following observations: 1) When the compound obtained was heated rapidly above 140° , there was vigorous decomposition, accompanied by a bang; 2) the substance decomposed with vigorous evolution of gas when mixed with concentrated hydrochloric acid, when added to silver oxide in a warm alcohol solution, or when the substance itself was added to boiling aniline.*

Our hypothesis on the diazomethene structure was confirmed by investigation of the infrared absorption spectrum. The spectrum contained a very strong absorption band in the region of 2060 cm^{-1} , close to the characteristic absorption band of diazomethane at 2109 cm^{-1} [6].

Evidently, the diazomethane derivative formed (IX) could not undergo ring closure to a bicyclic compound. In this compound, the tetrahedral carbon atom (shown by a point in the formula), attached to the benzoyl group, would make the structure of the heterocycles noncoplanar, producing considerable strain in the molecule.

Thus, in the interaction with diazomethane, the chloride (II) reacted not at the double bond, as assumed by Nesmeyanov and Kochetkov for the first stage of the reaction of a β -chlorovinyl ketone with diazomethane [3], but through its labile chlorine atom, like the acid chloride of a carboxylic acid.

In this connection it was of great interest to examine the absorption spectra in the double bond region. It was found that the valence oscillation of the carbonyl in compound (IX) equaled 1708 cm^{-1} and in the chloride (II), 1756 cm^{-1} instead of $1640\text{--}1670\text{ cm}^{-1}$ for carbonyls in aromatic ketones [7]. The data obtained indicate the great effect of the chlorine atom on the carbonyl and the similarity of the latter to the carbonyl of an acid chloride (for example, the oscillation frequency of the carbonyl in benzoyl chloride equals 1773 cm^{-1} [8]).

Compound (IX) may thus be regarded as a vinyllog of diazoketone. Correspondingly, the hydroxy derivative (I) and 3-methyl-4-benzoyl-5-aminoisoxazole (X) are vinyllogs of an acid and an amide. The hydroxy derivative shows acid characteristics and the amine (X), amide characteristics so clearly that Betti and Alessandri, who prepared these compounds for the first time, considered that the first compound was a carboxylic acid and the second, its amide [1, 9, 10]. The spectroscopic data, which are given in the table, correspond to the chemical behavior of these compounds.

EXPERIMENTAL

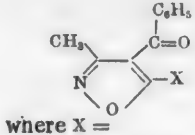
3-Methyl-4-benzoyl-5-chloroisoxazole (II). This compound was obtained by the method in [1] by treatment of 3-methyl-4-benzoyl-5-hydroxyisoxazole [10] with thionyl chloride with subsequent ligroine extraction. The yield was 60-70%. The m. p. was $93\text{--}95^\circ$ (according to data in [1], $93\text{--}95^\circ$).

3-Methyl-4-benzoyl-5-methylaminisoxazole (III). Anhydrous alcohol (10 ml) was saturated with methylamine. Then 0.5 g of 3-methyl-4-benzoyl-5-chloroisoxazole was added and the mixture boiled 10 minutes. After the solution had been evaporated to $1/3$ of its volume, water was added and the precipitated crystals collected. Coarse, colorless prisms were obtained from 50% alcohol. The yield was 0.42 g (86%) and the m. p. $163\text{--}164^\circ$.

Found %: C 66.45; H 5.31; N 13.22. $\text{C}_{12}\text{H}_{12}\text{O}_2\text{N}_2$. Calculated %: C 66.64; H 5.59; N 12.96.

*Analogous reactions have been described for diazo ketones [5].

Characteristic Absorption Bands in the Infrared Spectra of 3-Methyl-4-benzoyl-(X)-isoxazoles*

Compound no.	 where X =	Absorption bands (in cm ⁻¹)		Deductions from infrared spectral data
		assigned to X	assigned to carbonyl	
(I)	OH	3150 (w., diffuse)	1667 (s.)	Strong hydrogen bond between CO and OH groups
(II)	Cl		1756 (s.)	CO with properties of carbonyl in acid chloride
(IX)	$\text{CH}=\text{N}=\text{N}$ $\quad \quad \quad + \quad -$	2060 (v. s.)	1708 (s.)	Diazomethene group, carbonyl of diazoketone
(X)	NH ₂	3280 (s.) 3045 (s., broad)	1700 (s.)	Amide group, participating in hydrogen bond

* The spectra were plotted for the compounds in the crystalline state.

3-Methyl-4-benzoyl-5-(p-nitrophenylmercapto)-isoxazole (IV). A mixture of 0.5 g of 3-methyl-4-benzoyl-5-chloroisoxazole and 0.5 g of the sodium salt of p-nitrothiophenol in anhydrous alcohol was boiled for 2 hours. The precipitate was then collected and recrystallized from dioxane. It formed lustrous, yellow prisms. The yield was 0.6 g (72%) and the m. p. 217-220° (decomp.).

Found %: C 60.03; H 3.52; N 8.06. C₁₇H₁₂O₄N₂S. Calculated %: C 60.00; H 3.52; N 8.23.

3-Methyl-4,6-diphenylpyrazolo-[4,5-d]-isoxazole (V). a) To a solution of 0.37 g of phenylhydrazine in 10 ml of anhydrous alcohol was added 0.5 g of 3-methyl-4-benzoyl-5-chloroisoxazole and the solution boiled for 5 minutes. Then one half of the alcohol taken was removed by distillation and the solution cooled to 0°. The precipitate was recrystallized from alcohol. It formed colorless prisms. The yield was 0.55 g (80%) and the m. p. 183-184° (slight decomp.).

b) To a solution of 0.75 g of phenylhydrazine in 10 ml of water and 1.5 ml of glacial acetic acid was added 1.0 g of 3-methyl-4-benzoyl-5-hydroxyisoxazole and the mixture heated until solution was complete and then boiled for 2 hours. A precipitate rapidly began to form and the amount of it gradually increased. The yield was 1.2 g (88%) and the m. p. 184°. A mixed melting point with the sample obtained by method "a" was not depressed.

Found %: C 74.07; H 4.70; N 15.33. C₁₇H₁₃ON₃. Calculated %: C 74.12; H 4.75; N 15.27.

3-Methyl-4-phenylpyrazolo-[4,5-d]-isoxazole (VI). This was obtained analogously to compound (V) by method "a". It formed light yellow scales (from water). The yield was 55% and the m. p. 192-193° (decomp.).

Found %: C 66.27; H 4.55; N 21.27, 21.30. C₁₁H₉ON₃. Calculated %: C 66.30; H 4.52; N 21.10.

3-Methyl-4-phenyl-(6',7'-benzoheptadiazino-1',5')-[2,3-d]-isoxazole (VII). A mixture of 0.5 g of 3-methyl-4-benzoyl-5-chloroisoxazole and 0.3 g of o-phenylenediamine in 10 ml of anhydrous alcohol was boiled. The cooled solution was diluted with water and the precipitate collected. Recrystallization from butyl alcohol yielded fine, yellow prisms. The yield was 0.61 g (98%). The product decomposed when heated above 182°.

Found %: C 74.15; H 4.36; N 15.23, 15.24. C₁₇H₁₃ON₃. Calculated %: C 74.12; H 4.75; N 15.27.

3-Methyl-4-benzoyl-5-diazometheneisoxazole (IX). To a suspension of 1.0 g (0.0045 mole) of 3-methyl-4-benzoyl-5-chloroisoxazole in 10 ml of ether was added an ether solution of diazomethane, obtained from 1 g (0.0094 mole) of nitrosomethylurea. The reaction proceeded with the vigorous evolution of gas. The precipitate

which had formed after 15 minutes was collected and recrystallized from a mixture of benzene and ligroine (1 : 1). The yield was 0.70 g (68%). The decomp. p. was 136-138°. The compound formed fine, long, yellow needles. They darkened slightly in light.

Found %: C 63.20; H 4.23; N 18.43. $C_{12}H_9O_2N_3$. Calculated %: C 63.44; H 3.99; N 18.50.

The infrared spectra were plotted on an IKS-12 spectrograph with an LiF prism in the region 2.5-5 μ and with an NaCl prism from 5 to 12 μ . Absorption spectra are presented for compounds (I), (II), (III), (IV), (IX), and (X) in the crystalline state (2.5-7 μ in a perfluorinated hydrocarbon and from 7 to 12 μ in vaseline oil).*

(I) 3140 (w., diffuse), 2845 (w.), 1667 (s.), 1632 (s.), 1559 (s.), 1510 (s.), 1210 (av.), 1170 (w.), 1108 (av.), 1074 (w.), 1054 (w.), 1015 (av.), 970 (w.), 928 (w.), 898 (w.),

(II) 1756 (s.), 1594 (s.), 1230 (av.), 1140 (s.), 1020 (w.), 991 (w.), 885 (w.), 865 (w.),

(III) 1688 (s.), 1613 (av.), 1599 (w.),

(IV) 1724 (s.), 1599 (w.), 1565 (s.), 1520 (s.), 1270 (av.), 1220 (s.), 1165 (s.), 1108 (w.), 1077 (w.), 1048 (s.), 1012 (s.), 1005 (w.), 937 (w.), 898 (w.), 885 (w.), 865 (w.), 857 (w.),

(IX) 2060 (v.s.), 1708 (s.), 1165 (s.), 1148 (w.), 1115 (s.), 1030 (w.), 1012 (w.), 1005 (w.), 890 (w.), 875 (w.),

(X) 3270 (s.), 3035 (s., broad), 1700 (s.), 1653 (s.), 1606 (w.), 1250 (av.), 1165 (w.), 1130 (av.), 1040 (w.), 1010 (s.), 925 (w.), 890 (w.), 860 (w.).

The spectra were plotted by L. F. Trefilova.**

SUMMARY

1. It was shown that 3-methyl-4-benzoyl-5-chloroisoxazole reacts with phenylhydrazine, hydrazine hydrate, and o-phenylenediamine at the carbonyl group and the chlorine atom to form the condensed heterocyclic compounds V, VI, and VII.

2. It was established that by reaction with diazomethane, 3-methyl-4-benzoyl-5-chloroisoxazole forms a diazomethene instead of the expected pyrazoleisoxazole.

3. It was shown that 3-methyl-4-benzoyl-5-hydroxyisoxazole and its derivatives are vinylogs of acids and their derivatives. In the infrared spectra, the carbonyl bands of these compounds have the high valence oscillation frequency characteristic of carboxylic acids and their derivatives.

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* The spectra of (I) and (IX) were plotted in the region 2.5-12 μ , of (II), (IV), and (X) in the region 5-12 μ , and of (III), in the region 5-7 μ .

** The spectrum of the diazoketone (IX) was also plotted by Yu. N. Sheinker (VNIKhFI) and the authors are very grateful to him for this.

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DIAZO COMPOUNDS

XII. CONVERSIONS OF DIAZO ACETATE COMPOUNDS OF AMINOANTHRAQUINONES*

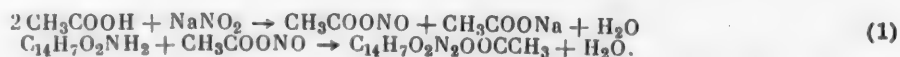
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Few conversions of diazo compounds of aminoanthraquinones with replacement of the diazo group by other substituents have been described in the literature [1].

Having established the possibility of smooth diazotization of aminoanthraquinones by dry nitrite or nitrosyl acetate (CH_3COONO) in acetic acid without the participation of a mineral acid and the high stability of such diazo solutions [2], we studied some conversions of diazo acetates of aminoanthraquinones.

For the conversions of diazo compounds, we used solutions of them in acetic acid, obtained by diazotization of the amine according to Scheme (I).



In addition, we also used solid diazo acetates, isolated from solution by means of diethyl ether. Some information on such solid diazo compounds is given in Table 1.

It should be pointed out that diazotization of aminoanthraquinones in acetic acid without mineral acid is not complicated by the formation of diazoamino compounds.

TABLE 1

Characteristics of Solid Diazo Acetates of Aminoanthraquinones, Isolated from Acetic Acid Solutions with Ether

Amino-anthra-quinones	Composition	Percent of diazo nitrogen		Characteristics of crystals	Flash point
		found	calculated		
α	$\text{C}_{14}\text{H}_7\text{O}_2\text{N}_2\text{OOCCH}_3$	9.75	9.52	Light brown, finely crystalline powder	120°
β	$\text{C}_{14}\text{H}_7\text{O}_2\text{N}_2\text{OOCCH}_3$	0.83	9.52	Grey-yellow, finely crystalline powder	160°
1,5-	$\text{C}_{14}\text{H}_6\text{O}_2[\text{N}_2\text{OOCCH}_3]_2$	14.86	14.73	Grey-brown, finely crystalline powder	159°
1,4-	$\text{C}_{14}\text{H}_6\text{O}_2[\text{N}_2\text{OOCCH}_3]_2$	14.94	14.73	The same	190°
1-Amino-4-nitro	$\text{C}_{14}\text{H}_6\text{O}_2\text{NO}_2\text{N}_2\text{OCOCH}_3$	8.69	8.22	Bright red, finely crystalline powder	173°

* For communication XI see Izvest. Vyssh. Uchebn. Zavedenií MVO, Ser. Khimiya i Khim. Tekhnologiya, 3, 374 (1959).

As with other salts of these diazo compounds, heating the acetates of diazoanthraquinones with water led to the formation of hydroxy compounds. However, due to the high stability of the various diazo compounds of aminoanthraquinones, replacement of the diazo by a hydroxy group proceeded slowly. Thus, we established that α -anthraquinonediazonium acetate was 90-92% converted into α -hydroxyanthraquinone after being heated for 4 hours in boiling water. The residue in solution was undecomposed diazo compound.

It seemed most interesting to replace the diazo group of diazo acetates of aminoanthraquinones by an acetoxy group.

If a solution of diazo compound, obtained by diazotization of aminoanthraquinone with dry sodium nitrite in glacial acetic acid, was boiled for a definite time, then a mixture of two substances, an acetoxy- and a hydroxyanthraquinone, was formed.

The conversion products of diazo compounds from α - and β -aminoanthraquinones and 1,5- and 1,4-diaminoanthraquinones, obtained after 4-hours heating in acetic acid, had a high content of acetoxy compound (89-90%) while the yield was an average of about 50% theoretical. The product yield would be raised by increasing the decomposition time of these stable diazo compounds. Due to the high content of acetoxy compound

TABLE 2

Conversion of a Solution of the Diazonium Acetate from α -Aminoanthraquinone in Acetic Acetate in Relation to Time (1 g of aminoanthraquinone, 30 ml of acetic acid, 118°)

Expt. no.	Time (in hours)	Product obtained		Yield (in %)	
		(in g)	acetoxyanthraquinone content (in %)	α -acetoxyanthraquinone	α -hydroxyanthraquinone
1	1	0.45	65	25.6	16.0
2	2	0.55	72	34.7	15.0
3	3	0.63	78	43.1	14.0
4	4	0.91	95	75.8	4.5

TABLE 3

Conversion of a Solution of the Diazonium Acetate from α -Aminoanthraquinone in Acetic Acid in Relation to Temperature (1 g of aminoanthraquinone, 30 ml of glacial acetic acid, 4 hours)

Expt. No.	Temperature	Product obtained		Yield (in %)	
		(in g)	acetoxyanthraquinone content (in %)	α -acetoxyanthraquinone	α -hydroxyanthraquinone
1	20°*	0.1	0.8	7.0	2.0
2	50	0.23	45.0	9.0	13.0
3	100	0.74	65.0	42.1	26.0
4	118	0.91	95.0	75.8	4.5
5	118	0.9	93.6	74.5	6.0**
6	118	0.96	96.0	80.8	4.0***

* Decomposition carried out for 1 month in the dark.

** With 2.5 g of sodium acetate.

*** With 1 ml of acetic anhydride.

in the crude product, it was obtained readily in a pure form by recrystallization. In this the given method had an appreciable advantage over known methods of converting mineral salts of diazo compounds in acetic acid [3].

Complete conversion of the diazo compound required the optimal conditions for each aminoanthraquinone. Apart from time (Table 2), an important factor in the conversion of the diazo compound in acetic acid was temperature.

According to the example of the diazotized α -aminoanthraquinone, a high boiling point of the solvent (Table 3) and a long heating time (Table 2) promoted replacement of the diazo group by an acetoxy group and reduced the yield of hydroxyanthraquinone. The data in Table 2 show that with an increase in the heating time the yield of hydroxyanthraquinone remained constant. This circumstance and also the fact that α -acetoxyanthra-

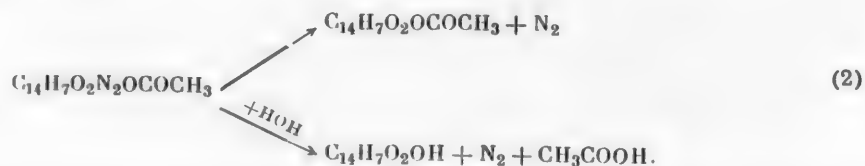
TABLE 4

Conversion of Solid Diazonium Acetate from α -Aminoanthraquinone in Acetic Acid in Relation to Time (1 g of α -anthraquinonediazonium acetate, 50 ml of glacial acetic acid, 100°)

Experiment No.	Time (in hours)	Percent conversion of diazo compound*
1	0.5	28.35
2	1.0	56.8
3	2.0	72.5
4	3.0	84.35
5	4.0	90.2

* Determined by coupling the residual diazonium compound with excess 0.05 N β -naphthol solution and titrating the latter with 0.05 N solution of p-nitrobenzene-diazonium chloride.

quinone is not hydrolyzed appreciably in acetic acid indicated that the formation of acetoxyanthraquinone and hydroxyanthraquinone during the decomposition of α -anthraquinonediazonium acetate in acetic acid occurs simultaneously according to Scheme (2).



The formation of the hydroxyanthraquinone from the diazo compound is apparently caused by water which appears in the acetic acid during diazotization of the aminoanthraquinone according to Scheme (1).

Heating the diazo compound in acetic acid with sodium acetate or acetic anhydride added produced some increase in the yield of acetoxy compound, while the amount of hydroxyanthraquinone remained unchanged (Table 2). The increase in yield of the acetoxy compound was the result of binding of the water by the additives.

The hypothesis that acetoxyanthraquinone might have been formed from hydroxyanthraquinone and the acetic anhydride added to the acetic acid was not confirmed either by separate experiments (the acetoxy compound yield was a maximum of 5%) or by the known difficult acetylation of hydroxy derivatives of anthraquinone [4].

When we heated α -hydroxyanthraquinone for 6 hours with a large excess of acetic anhydride (30-50 ml of anhydride to 1 g of hydroxyanthraquinone), only 45% of the starting material was acetylated. According to our observations, hydroxyanthraquinones are acetylated quantitatively by acetic anhydride only when 30-40% of pyridine is added.

We also decomposed solid α -anthraquinonediazonium acetate in other solvents: Acetic anhydride, dry acetone, dioxane, benzene, cyclohexane, tetralin, and pyridine. Decomposition in acetic anhydride, acetone, and especially dioxane and pyridine led to pure α -acetoxyanthraquinone in yields of from 72 to 94%.

TABLE 5

Conversion of Solid Diazonium Acetate from α -Aminoanthraquinone in Various Media (1 g of α -anthraquinone-diazonium acetate, 30 ml of solvent, 4 hours)

Expt. No.	Medium	Decomposition temperature	Product obtained (in g)	Melting point	Yield (in %)		
					α -acetoxy-anthra-quinone	α -hydroxy-anthra-quinone	anthra-quinone
1	Water	100°	0.66	191°	None	91.6	None
2	Dioxane	100	0.8	178	87.0	None	None
3	Pyridine	115	0.86	179	94.0	None	None
4	Acetic acid	118	0.75	169	79.0	5.2	None
5	Acetic anhydride	140	0.68	178	75.5	None	None
6	Benzene	80	0.63	222	32	6.3	2.5*
7	Acetone	56	0.89	174	72.2	None	None
8	Cyclohexane	80	0.58	198	45	7.2	3.0*
9	Tetralin	207	Considerable tar formation, products not isolated				
10	Nitrobenzene	208	Considerable tar formation, products not isolated				

* Decomposition accompanied by tar formation.

Decomposition in tetralin and nitrobenzene, which was carried out at the boiling points of these solvents (207-208°), was complex with the formation of a viscous, tarry mass. About 5.6% of acetoxyanthraquinone was found in the product from tetralin, but the compound was absent from the product from nitrobenzene.

Decomposition in benzene and cyclohexane at 80° led to the formation of partly tarry products from which we were able to isolate α -acetoxyanthraquinone (22-30%) and anthraquinone (2.5-3.0%).

Thus, it can be stated that the results of decomposition of α -anthraquinonediazonium acetate depend on temperature and the nature of the solvent.

The smooth formation of α -acetoxyanthraquinone during reaction in acetone, acetic anhydride, and dioxane, uncomplicated by the formation of side-products (anthraquinone, CO₂, etc.), does not make it possible to assume a homolytic mechanism for the decomposition of diazo acetates in these cases [5].

Considering the different direction of the conversion of α -anthraquinonediazonium acetate in benzene and cyclohexane, it should be assumed that temperature, the nature of the nonpolar solvent, and the nature of the diazo compound are of importance in homolytic decomposition of diazo acetates.

EXPERIMENTAL*

Diazotization and conversion of diazoanthraquinones in acetic acid. 1. A sample of 1 g of α -aminoanthraquinone (m. p. 240°) was dissolved in 30 ml of glacial acetic acid by 1-2-minutes boiling, filtered through a hot funnel, cooled to 30-40°, and diazotized by stirring with 0.5 g of dry sodium nitrite. The solution was stirred for 30 minutes, the excess nitrite destroyed with urea, and the solution used for decomposition (when added to water, a drop of the diazo acetate solution should not give turbidity due to unchanged amine). The diazo solution was placed in a round-bottomed flask with a reflux condenser and a calcium chloride tube and boiled for a definite time (up to 4 hours) on a mantle. The solution was cooled and poured into 400 ml of ice water. The yellow precipitate was rapidly collected, washed with ice water, and dried at 60°. The yield of product was 0.85 g and the m. p. 176-180°; after recrystallization from alcohol, the substance melted at 178° and did not depress the melting point of pure α -acetoxyanthraquinone [6].

A portion of 0.1263 g of the crude product was heated for 4 hours on a boiling water bath in 20 ml of 0.1 N alcoholic KOH in a round-bottomed flask with a reflux condenser. The excess caustic alkali in the cooled solution was titrated with 0.1 N HCl with a LP-8 potentiometer. We found 95% of acetoxy compound, representing a yield of 71.1%.

2. A sample of 1 g of β -aminoanthraquinone (m. p. 301°) in 50 ml of glacial acetic acid was diazotized and then decomposed as in the previous case. We obtained 0.73 g of product with m. p. 164° and an acetoxy compound content of 89.5%, which corresponds to a yield of 57.2%. After recrystallization from alcohol, the substance melted at 160° and did not depress the melting point of pure β -acetoxyanthraquinone [7].

3. A sample of 1 g of 1,5-diaminoanthraquinone (m. p. 318°) in 30 ml of glacial acetic acid was diazotized and then decomposed as in the previous case. We obtained 0.62 g of product with m. p. 250° and an acetoxy compound content of 89.6%, which corresponds to a yield of 41.1%. After recrystallization from acetic acid, the substance had m. p. 246°, which corresponds to that of pure 1,5-diacetoxyanthraquinone [8].

4. A sample of 1 g of 1,4-diaminoanthraquinone (m. p. 258°) in 30 ml of glacial acetic acid was diazotized and then decomposed as previously. We obtained 0.8 g of product with m. p. 201-203° and an acetoxy compound content of 99.8%, which corresponds to a yield of 58.8%. After recrystallization from 60% acetic acid, the substance had m. p. 198°, which corresponds to that of pure 1,4-diacetoxyanthraquinone [8].

The diazo acetates from aminoanthraquinones, which we described previously in the form of their binary salts with mercuric chloride [1], were isolated in the solid state by treatment of the acetic acid solution with a 3-fold volume of diethyl ether. Under these conditions, up to 50% of the diazo compound contained in the solution was precipitated as a finely crystalline powder, which was collected, washed with ether, dried in a vacuum desiccator over KOH with continuous pumping in the dark. The anthraquinonediazonium acetates were readily soluble in water and coupled readily with various azo components.

Conversions of α -aminoanthraquinonediazonium acetate. 1. A sample of 1 g of solid α -anthraquinonediazonium acetate in 30 ml of solvent was boiled in a flask with a reflux condenser and a calcium chloride tube for 4 hours. After distillation of the bulk of the solvent, the reaction mixture was poured into water and treated as described above.

2. The dry reaction product was treated as follows: One part was analyzed for the acetoxy compound content and the other was treated with a 5% solution of K_2CO_3 in the cold for 5 minutes. The soluble part was separated and the residue on the filter washed and dried.

Acidification of the alkaline solution with hydrochloric acid liberated α -hydroxyanthraquinone (m. p. 190-193°). After recrystallization from alcohol, the alkali-insoluble residue was found to be α -acetoxyanthraquinone (m. p. 176-179°). The alcohol-insoluble residue sublimed readily and showed all the properties of anthraquinone (m. p. 285°). Anthraquinone was also readily separated from acetoxyanthraquinone by sublimation when the crude product (from decomposition of α -anthraquinonediazonium acetate in benzene and cyclohexane) was heated.

* With the participation of N. I. Semenova.

SUMMARY

1. It was established that the diazo group in diazo acetates from aminoanthraquinones may be replaced smoothly by the acetoxy group.
2. It was established that the nature and degree of conversion of diazo acetates from aminoanthraquinones depend on temperature, time, and the nature of the solvent.
3. Solid diazo acetates from some aminoanthraquinones were isolated and characterized.

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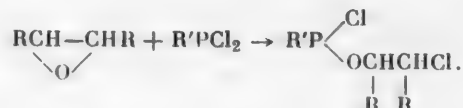
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METHOD OF PREPARING 2-CHLOROALKYL ESTERS OF ALKYLCHLOROPHOSPHINOUS ACID

S. Z. Ivin and K. V. Karavanov

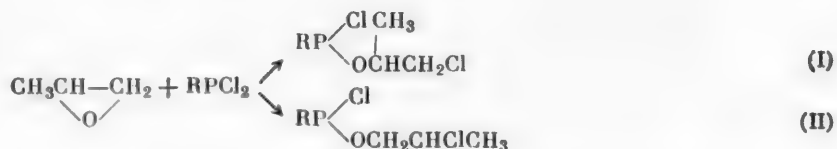
2-Chloroalkyl esters of alkylchlorophosphinous acid have not been described in the literature before our investigation. We found a method of preparing them which consisted of reacting alkylidichlorophosphines with alkylene oxides. Thus, when an alkylene oxide was introduced into an ether solution of alkylidichlorophosphine, the reaction began immediately and the three-membered oxide ring of the alkylene oxide was opened to form the corresponding ester acid chloride of the alkylphosphinous acid according to the scheme



Methyl- and ethyldichlorophosphines were reacted with ethylene, propylene, and cyclohexene oxides. The yield of the final products reached 70%.

Sulfur was added to the 2-chloroethyl and 2-chloropropyl methylchlorophosphinites obtained by this method. The substances isolated were 2-chloroethyl and 2-chloropropyl methylchlorothiophosphinates, respectively. This showed that the reaction products of alkylene oxides and alkylidichlorophosphines were compounds of trivalent phosphorus, capable of adding sulfur.

The reaction of propylene oxide with alkylidichlorophosphines, described in the present work, may proceed in two directions, namely, with the formation of 2-chloroisopropyl alkylchlorophosphinite (I), 2-chloro-n-propyl alkylchlorophosphinite (II), or a mixture of the two.





The structure of the product we obtained was not studied. However, it is known that hydrogen chloride [1] and acid chlorides of carboxylic acids [2] open the oxide ring of propylene oxide in such a way that the oxygen of the oxide ring remains attached to the central carbon atom and the chlorine adds to the terminal carbon atom so that an O-2-chloroisopropyl radical is formed as a result.

This gives grounds for considering that cleavage of the oxide ring of propylene oxide with alkylidichlorophosphines proceeds largely in the first direction with the formation of substance (I).

EXPERIMENTAL

The alkylene oxides were cleaved by alkylidichlorophosphines by a single procedure. Into a Claisen flask with a pear column were placed 0.1 mole of alkylidichlorophosphine and 35-40 ml of absolute ether. Then 0.12

Expt. No.	Starting materials	Compound formed	Boiling point (pressure in mm)	d_4^{18}	n_D^{18}	Found (%)		Calculated (%)		Yield (in %)
						P	Cl	P	Cl	
1	$\text{CH}_2=\text{CH}_2\text{O}$, CH_3PCl_2	$\text{CH}_3\text{P}(\text{Cl})\text{OCH}_2\text{CH}_2\text{Cl}$	59-60° (12)	1.2699	1.495			19.24	44.1	64.0
2	$\text{CH}_3\text{CHCH}_2\text{O}$, CH_3PCl_2	$\text{CH}_3\text{P}(\text{Cl})\text{OCH}_2\text{CH}_2\text{Cl}$	56-57° (6-7)	1.1985	1.483	19.30	44.4	17.7	40.6	73.0
3	$\text{CH}_2=\text{CH}_2\text{O}$, $\text{C}_2\text{H}_5\text{PCl}_2$	$\text{C}_2\text{H}_5\text{P}(\text{Cl})\text{OCH}_2\text{CH}_2\text{Cl}$	75 (15)	1.2152	1.490	17.60	39.8	17.7	40.6	44.5
4	$\text{CH}_3\text{CH}(\text{CH}_3)\text{O}$, $\text{C}_2\text{H}_5\text{PCl}_2$	$\text{C}_2\text{H}_5\text{P}(\text{Cl})\text{OCH}_2\text{CH}_2\text{Cl}$	80 (7)	1.1900	1.4810	16.5	36.95	16.50	37.5	52.0
5	 , $\text{C}_2\text{H}_5\text{PCl}_2$		132 (10)	1.200 (at 13°)	1.5080 (at 13°)	13.40	31.30	13.60	31.00	54.0

mole of alkylene oxide was introduced at 0-5°. Twenty to twenty-five minutes after all the alkylene oxide had been added, the ether was evaporated and the ester acid chloride of the alkylphosphinous acid formed was vacuum distilled. The experimental results are given in the table.

2-Chloroethyl methylchlorothiophosphate. Into a Claisen flask with a pear column, previously flushed with carbon dioxide, was placed 8.0 g of 2-chloroethyl methylchlorophosphinite. Then 1.6 g of sulfur was gradually added. The mixture was heated at 45° for 30 minutes to complete the reaction and then fractionally distilled. We obtained 7.6 g (77%) of substance.

B. p. 95-96° at 10 mm, d_4^{18} 1.3647, n_D^{18} 1.518.

Found %: Cl 36.59; P 16.03; S 16.64. $\text{C}_3\text{H}_7\text{OSPCL}_2$.
Calculated %: Cl 36.78; P 16.05; S 16.57.

2-Chloropropyl methylchlorothiophosphate. The experiment was similar to the previous one. From 8.7 g of 2-chloropropyl methylchlorophosphinite and 1.6 g of sulfur we obtained 8.5 g (82%) of substance.

B. p. 94-95° at 6 mm, d_4^{20} 1.2908, n_D^{20} 1.510.

Found %: Cl 34.31; P 14.86; S 15.29. $\text{C}_4\text{H}_9\text{OSPCL}_2$.
Calculated %: Cl 34.28; P 14.86; S 15.49.

SUMMARY

1. A new method was found for preparing 2-chloroalkyl esters of alkylchlorophosphinous acid by interaction of alkyl-dichlorophosphines with alkylene oxides.

2. 2-Chloroethyl and 2-chloropropyl methylchlorophosphinites, 2-chloroethyl, 2-chloropropyl, and 2-chlorocyclohexyl ethylchlorophosphinites, and 2-chloroethyl and 2-chloropropyl methylchlorothiophosphates were prepared and characterized.

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ARYLAMINOLYSIS OF ARYL PHENYLDICHLOROPHOSPHAZOSULFONES

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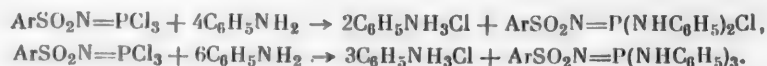
Dnepropetrovsk Metallurgical Institute

Aryl phenyldichlorophosphazosulfones (I), which were described in a previous communication [1], are analogs of aryl trichlorophosphazosulfones (II), in which one of the chlorine atoms had been replaced by a phenyl radical.

To determine the effect of replacement of the chlorine atom by a phenyl radical on the chemical properties of phosphazo compounds, it seemed interesting to compare the reaction characteristics of aryl phenyldichloro- and trichlorophosphazosulfones and also the properties of the products thus obtained.

Reactions of aryl trichlorophosphazosulfones with aniline, ammonia, and other compounds have been described in the literature [2].

Aryl trichlorophosphazosulfones react with aniline in such a way that it is possible to isolate only the products of replacement of two or three chlorine atoms.



It was not possible to isolate the products from replacement of one chlorine atom by an aniline residue even with a large excess of (II).

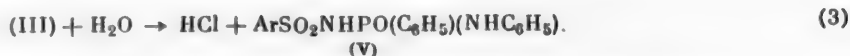
It might have been expected that in the reaction of aryl phenyldichlorophosphazosulfones with aniline, two atoms of chlorine would also react immediately. However, it was found that one of the chlorine atoms in aryl phenyldichlorophosphazosulfones reacted with aniline much more readily than the other and depending on the ratio of the reagents, it was easy to obtain either aryl phenylanilinochlorophosphazosulfones (III).



or aryl phenyldianilinophosphazosulfones (IV).



The action of two moles of aniline on one mole of (I) in a benzene solution formed (III), which were colorless, crystalline substances, readily hydrolyzed by water. In the given work, (III) were not isolated in a pure form; by hydrolysis with water or sodium hydroxide solution they were converted into monoanilides of aryl-sulfonamidophenylphosphinic acids (V) according to the scheme:



Substances (V) were colorless crystals which were readily soluble in acetone, more difficultly so in hot alcohol, and insoluble in water, ether, benzene, and carbon tetrachloride. They crystallized from alcohol in the

form of long, fine needles. From a chemical point of view, the monoanilides were monobasic acids, which were titrated by one equivalent of an aqueous solution of sodium hydroxide (in the presence of phenolphthalein).

Table 1 gives the yields, melting points, and analysis data of monoanilides of arylsulfonamidophenylphosphinic acids, obtained by Schemes (1) and (3).

TABLE 1

Monoanilides of Arylsulfonamidophenylphosphinic Acids
 $\text{ArSO}_2\text{NHPO}(\text{C}_6\text{H}_5)(\text{NHC}_6\text{H}_5)$

Substance No.	Ar	Yield (in %)	Melting point	Empirical formula	Equivalent	
					found	calc.
(VI)	C_6H_5	62.5	167°	$\text{C}_{18}\text{H}_{17}\text{O}_3\text{N}_2\text{SP}$	0.99	1.00
(VII)	$\alpha\text{-C}_{10}\text{H}_7$	70.2	169	$\text{C}_{22}\text{H}_{19}\text{O}_3\text{N}_2\text{SP}$	1.00	1.00
(VIII)	$\text{-NO}_2\text{C}_6\text{H}_4$	63.5	165	$\text{C}_{18}\text{H}_{16}\text{O}_5\text{N}_3\text{SP}$	0.99	1.00
(IX)	$\text{m-NO}_2\text{C}_6\text{H}_4$	83.2	169	$\text{C}_{18}\text{H}_{16}\text{O}_5\text{N}_3\text{SP}$	0.99	1.00
(X)	$\text{p-NO}_2\text{C}_6\text{H}_4$	79.3	166	$\text{C}_{18}\text{H}_{16}\text{O}_5\text{N}_3\text{SP}$	1.02	1.00

While one of the two chlorine atoms in aryl phenyldichlorophosphazosulfones was readily replaced by an anilino group [Reaction (1) proceeded even at room temperature when benzene solutions of the reagents were mixed], replacement of the other chlorine atom by an aniline residue was very difficult. Thus, when a benzene solution of 5 moles of aniline and 1 mole of aryl phenyldichlorophosphazosulfone was heated on a boiling water bath for 8 hours the reaction did not proceed to completion and considerable amounts of (III) (up to 30%) were obtained as intermediate products.

The difficulty of replacing the last chlorine atom in both aryl trichloro- and phenyldichlorophosphazosulfones by an anilino group is undoubtedly explained by steric factors. For example, this is confirmed by the fact that in the reaction with ammonia, all the chlorine atoms are readily replaced by the amino group, which has a smaller volume, while diethylamine, which has a larger effective volume, reacts similarly to aniline.

TABLE 2

Aryl Phenyldianilinophosphazosulfones $\text{ArSO}_2\text{N}=\text{P}(\text{C}_6\text{H}_5)(\text{NHC}_6\text{H}_5)_2$
 (IV)

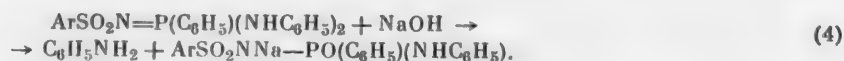
Substance No.	Ar	Yield (in %)	Melting point	Empirical formula	% N	
					found	calc.
(XI)	C_6H_5	85.6	191	$\text{C}_{24}\text{H}_{22}\text{O}_2\text{N}_3\text{SP}$	9.50	9.39
(XII)	$\text{-CH}_3\text{C}_6\text{H}_4$	71.2	196	$\text{C}_{25}\text{H}_{24}\text{O}_2\text{N}_3\text{SP}$	9.10	9.11
(XIII)	$\text{p-CH}_3\text{C}_6\text{H}_4$	70.6	182	$\text{C}_{25}\text{H}_{24}\text{O}_2\text{N}_3\text{SP}$	8.95	9.11
(XIV)	$\alpha\text{-C}_{10}\text{H}_7$	85.3	207	$\text{C}_{26}\text{H}_{24}\text{O}_2\text{N}_3\text{SP}$	8.29	8.45
(XV)	$\beta\text{-C}_{10}\text{H}_7$	88.3	215	$\text{C}_{28}\text{H}_{24}\text{O}_2\text{N}_3\text{SP}$	8.50	8.45
(XVI)	$\text{-NO}_2\text{C}_6\text{H}_4$	79.8	212	$\text{C}_{24}\text{H}_{21}\text{O}_4\text{N}_4\text{SP}$	11.21	11.38
(XVII)	$\text{m-NO}_2\text{C}_6\text{H}_4$	79.8	214	$\text{C}_{24}\text{H}_{21}\text{O}_4\text{N}_4\text{SP}$	11.24	11.38
(XVIII)	$\text{p-NO}_2\text{C}_6\text{H}_4$	96.0	176	$\text{C}_{24}\text{H}_{21}\text{O}_4\text{N}_4\text{SP}$	11.19	11.38

Table 2 gives the yields, melting points, and analysis data of aryl phenyldianilinophosphazosulfones (IV).

Aryl phenyldianilinophosphazosulfones were colorless, crystalline substances, which were readily soluble in acetone, comparatively difficultly so in boiling alcohol, and insoluble in water, ether, and benzene. They were very stable in acid and neutral media and remained unchanged even during prolonged boiling with a 0.2 N aqueous alcohol solution of hydrochloric acid. (IV) were less stable in alkaline media and were converted into

sodium salts of monoanilides of arylsulfonamidophenylphosphinic acids by Scheme (4) or more complex products of undetermined structure.

The nature of the aromatic radical attached to the sulfone group had a large effect on the rate and direction of the hydrolysis of aryl phenyldianilinophosphazosulfones in an alkaline medium. Thus, phenyl (XI), p-tolyl (XIII), and β -naphthyl (XV) phenyldianilinophosphazosulfones were hydrolyzed comparatively readily by 0.2 N aqueous alcohol solution of sodium hydroxide (heating for 8 hours) to form sodium salts of monoanilides of arylsulfonamidophenylphosphinic acids according to the scheme:



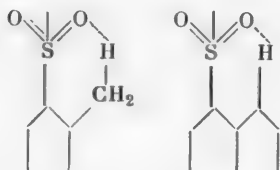
In contrast to (XI), (XIII), and (XV), o-tolyl (XII) and α -naphthyl (XIV) phenyldianilinophosphazosulfones were not hydrolyzed by a 0.2 N aqueous alcohol solution of sodium hydroxide, even on very prolonged boiling. They were only hydrolyzed under more drastic conditions, namely, heating (8-10 hours) with a 2 N alcohol solution of sodium hydroxide.

On the other hand, nitro derivatives, namely o-, m-, and p-nitrophenyl phenyldianilinophosphazosulfones (XVI), (XVII), and (XVIII), changed very readily when heated in an alkaline medium. However, in this case it was impossible to isolate the corresponding monoanilides of nitrophenylsulfonamidophenylphosphinic acids (VIII), (IX), and (X). Acidification of the hydrolyzate precipitated resinous, colored products of undetermined structure.

Attention is attracted by the difficulty of hydrolysis of the o-tolyl and α -naphthyl derivatives (XII) and (XIV). The o-tolyl and α -naphthyl derivatives also show distinctive characteristics in other compounds of a similar type.

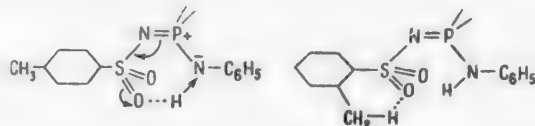
Thus, for example, in tri-o-nitrophenyl esters of the general form $\text{ArSO}_2\text{N}=\text{P}(\text{OC}_6\text{H}_4\text{NO}_2-\text{o})_3$ the compounds with $\text{Ar} = \text{o-CH}_3\text{C}_6\text{H}_4$ and $\alpha\text{-C}_{10}\text{H}_7$ have considerably higher melting points, lower solubility, and other distinctive properties [3].

To explain these peculiarities, the hypothesis was put forward that since in these compounds the position in the nucleus ortho to the sulfonyl group is substituted, there is the possibility of the formation of a hydrogen bond with the oxygen atoms attached to the sulfur.

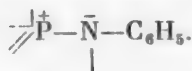


This fact is interesting in that it makes it possible to put forward a hypothesis on the mechanism of the hydrolysis of aryl phenyldianilinophosphazosulfones (IV).

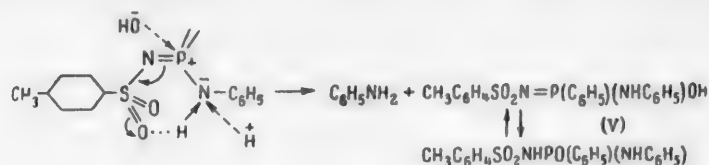
The structure of (IV) with free and substituted ortho positions may be represented by the example of o- and p-tolyl phenyldianilinophosphazosulfones with the following formulas:



As a result of the formation of a hydrogen bond, involving the hydrogen of an anilino group and displacement of an electron pair, in the para derivative there is formed a six-membered ring with the dipole



The transition state, formed as a result of the attack of a hydroxyl group on the positively charged phosphorus, decomposes with the formation of (V).



With *o*-tolyl or α -naphthyl phenyldianilinophosphazosulfone, the formation of a hydrogen bond through the hydrogen of the anilino group is hindered by the formation of a "competing" hydrogen bond through the hydrogen of the ortho substituent. As a result, the magnitude of the charge on the positive end of the dipole is decreased and the attack of a hydroxyl ion on the phosphorus atom is hindered so that a larger concentration of OH ions is required and they need a higher energy to establish an analogous transition state.

Table 3 gives the yields, melting points and analysis data of monoanilides of arylsulfonamidophenylphosphinic acids (V), obtained by alkaline hydrolysis.

TABLE 3

Monoanilides of Arylsulfonamidophenylphosphinic Acids (V)
 $\text{ArSO}_2\text{NH} - \text{PO}(\text{C}_6\text{H}_5)(\text{NHC}_6\text{H}_5)$, Obtained by Alkaline Hydrolysis

Sub- stance No.	Ar	Yield (in %)	Melt- ing point	Empirical formula	Equivalent	
					found	calc.
(VI)	C_6H_5	67.2	167°	$\text{C}_{18}\text{H}_{17}\text{O}_3\text{N}_2\text{SP}$	0.99	1.00
(VII)	$\alpha\text{-C}_{10}\text{H}_7$	59.2	164	$\text{C}_{22}\text{H}_{19}\text{O}_3\text{N}_2\text{SP}$	1.01	1.00
(XIX)	$\text{o-CH}_3\text{C}_6\text{H}_4$	37.0	164	$\text{C}_{19}\text{H}_{19}\text{O}_3\text{N}_2\text{SP}$	1.00	1.00
(XX)	$\text{p-CH}_3\text{C}_6\text{H}_4$	59.4	160	$\text{C}_{19}\text{H}_{19}\text{O}_3\text{N}_2\text{SP}$	1.01	1.00
(XXI)	$\beta\text{-C}_{10}\text{H}_7$	47.3	164	$\text{C}_{22}\text{H}_{19}\text{O}_3\text{N}_2\text{SP}$	1.03	1.00

The monoanilides of arylsulfonamidophenylphosphinic acids (V), obtained by hydrolysis according to Scheme (4) and by hydrolysis of (III) according to Scheme (3), were quite identical and did not differ in physical or chemical properties.

EXPERIMENTAL

Preparation of aryl phenyldianilinophosphazosulfones (IV). A solution of 0.003 mole of (I) in 5 ml of dry benzene was added to 0.015 mole of aniline in 5 ml of benzene. As a result of a weakly exothermal reaction a precipitate formed. The mixture was boiled for 5-8 hours. The precipitate was collected and washed with water to remove aniline hydrochloride; at the same time, (III), which was formed as an intermediate product, was hydrolyzed. The precipitate was then washed with 1 N sodium hydroxide solution to remove (V) and again with water. The (IV) remaining on the filter was recrystallized from alcohol. Data on (IV) are given in Table 2.

Acidification of the wash waters to Congo precipitated (V), which was collected and purified by recrystallization from alcohol.

Preparation of monoanilides of arylsulfonamidophenylphosphinic acids (V). To a solution of 0.002 mole of (I) in 10 ml of dry benzene was added a solution of 0.04 mole of aniline in 5 ml of benzene with stirring. To complete the reaction, the mixture was boiled for 2-3 hours. In the preparation of (V) from nitrophenyl phenyldichlorophosphazosulfones [*o*-, *m*-, and *p*- $\text{NO}_2\text{C}_6\text{H}_4\text{SO}_2\text{N} = \text{P}(\text{C}_6\text{H}_5)_2$], the substances (III) formed were sparingly soluble in benzene and formed a precipitate which was collected and hydrolyzed directly on the filter by washing it several times with water; aniline hydrochloride was also removed by this treatment. The (V) remaining on the filter was recrystallized from alcohol.

In the formation of phenyl or α -naphthyl phenylanilinochlorophosphazosulfones, the substances (III) obtained were readily soluble in benzene. After removal of the aniline hydrochloride precipitate, the benzene filtrate was evaporated and the crystalline residue (III) hydrolyzed by washing several times with water.

The substances (V) obtained thus are given in Table 1.

Hydrolysis of aryl phenyldianilinophosphazosulfones. To 0.001 mole of (XI), (XIII), or (XV) was added 25 ml of a 0.2 N aqueous alcohol solution of sodium hydroxide (5 ml of 1 N NaOH + 20 ml of alcohol), the solution boiled for 8 hours, and then the alcohol removed by distillation. The unreacted starting materials (XI), (XIII), or (XV) which precipitated on cooling were removed by filtration and the monoanilides (VI), (XX), and (XXI) precipitated by acidification of the filtrate.

Compounds (XII) and (XIV) were hydrolyzed in exactly the same way but a 2 N alcohol solution of sodium hydroxide was used instead of a 0.2 N aqueous alcohol solution. After removal of the alcohol, acidification of the hydrolyzate precipitated the monoanilides (VII) and (XIX) which were recrystallized from alcohol.

The monoanilides of phenylsulfonamidophenylphosphinic acids obtained in this way are listed in Table 3.

SUMMARY

1. The reaction of aryl phenyldichlorophosphazosulfones with aniline was studied. Aryl phenyldianilino-phosphazosulfones were synthesized.
2. The alkaline hydrolysis of aryl phenyldianilinophosphazosulfones was studied. Hydrolysis of aryl phenyldianilino- and phenylanilinochlorophosphazosulfones yielded monoanilides of arylsulfonamidophenylphosphinic acids.

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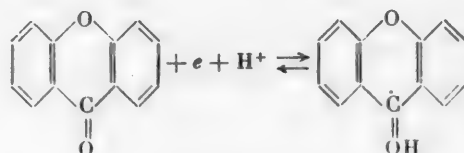
* Original Russian pagination. See C. B. Translation.

POLAROGRAPHY OF SOME DERIVATIVES OF THIOXANTHENE 5-DIOXIDE

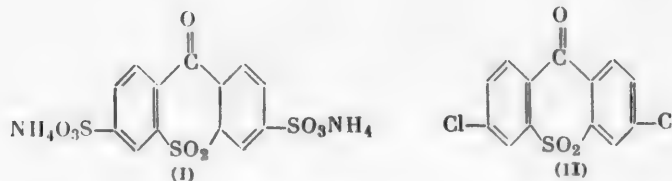
I. A. Korshunov and N. I. Malyugina

Scientific Research Institute of Chemistry, Gor'kii State University

In the present work, some derivatives of thioxanthene 5-dioxide with indicator properties* were investigated. The polarographic behavior of xanthone and methoxyxanthenes, which are compounds of a similar type, has been investigated [2, 3]. When reduced at a dropping mercury electrode, these compounds gave a single wave and the half-wave potential of xanthone in buffer solutions changed from -0.84 to -1.45 v when the pH value was increased from 1.0 to 12.7. According to the conclusions of the authors of the work cited above, the reduction of xanthone and methoxyxanthenes is a one-electron reversible process with the formation of a free radical and proceeds according to the scheme:



We studied the polarographic reduction on a mercury dropping electrode of the ammonium and sodium salts of thioxanthonedisulfonic acid dioxide (I) and 3,7-dichlorothioxanthone 5-dioxide (II), which have the following structures:



The polarograms were plotted on an electronic integrating-differentiating polarograph [4], with which it was possible to plot both normal integral curves in the coordinates $i-E$ and also differential curves in the coordinates $\frac{di}{dE} - E$.

The half-wave potential was measured relative to a saturated calomel electrode. For the investigations we used base electrolytes of various neutral salts, acids, alkalis, and buffer solutions. Due to the insolubility of 3,7-dichlorothioxanthone 5-dioxide in water, it was reduced in the presence of 40-60% alcohol after the solutions had been carefully freed from dissolved oxygen.

In base electrolytes of LiCl , KNO_3 , Na_2SO_4 , and HCl , the sodium and ammonium salts of thioxanthonedisulfonic acid dioxide gave well-expressed waves with half-wave potentials which agreed for the two compounds within the limits of experimental error (Table 1).

As the data in Table 1 show, in solutions of neutral salts the half-wave potentials had practically the same values, while in hydrochloric acid solution the half-wave potential was displaced in a positive direction.

*Synthesized by V..S. Étlis [1] and kindly placed at our disposal.

TABLE 1

Half-wave Potential and Diffusion Current of Ammonium and Sodium Salts of Thioxanthone Dioxide in Various Media

Base electrolyte	Sodium salt of thioxanthone dioxide, 0.002 M		Ammonium salt of thioxanthone dioxide, 0.006 M	
	$E_{1/2}$ (in v)	i_d (in μ a)	$E_{1/2}$ (in v)	i_d (in μ a)
0.2 N LiCl	-0.73	10.5	-0.72	28.80
0.2 N KNO ₃	-0.71	10.5	-0.73	28.56
0.2 N Na ₂ SO ₄	-0.73	10.7	-0.72	28.32
0.2 N HCl	-0.37	11.0	-0.39	29.76
0.2 N NaOH	-0.70; -0.91	11.65*	-0.71; -0.92	28.32*

* Total value.

In contrast to the behavior of these compounds in acid and neutral solutions, the ammonium (sodium) salt of thioxanthonosulfonic acid dioxide formed two diffusion waves when reduced in sodium hydroxide solution (Fig. 1, Curve 5).

It should be noted that small changes in the base electrolyte concentration (from 0.1 to 0.6 M) had no appreciable effect on the nature of the reduction.

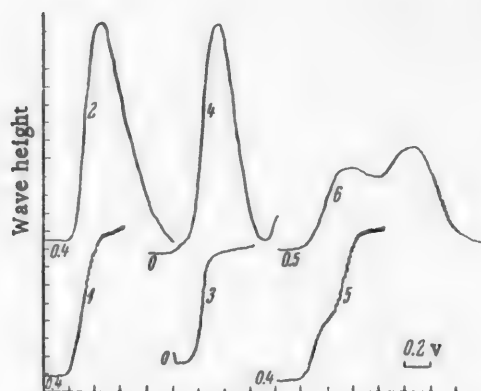


Fig. 1. Integral and differential curves of the ammonium salt of thioxanthonosulfonic acid dioxide (concentration 0.002 M) on KNO₃ (Curves 1 and 2), HCl (Curves 3 and 4), and NaOH (Curves 5 and 6*) base electrolytes.

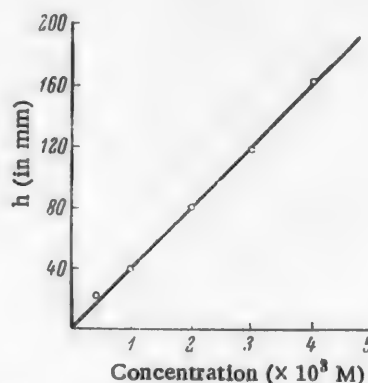


Fig. 2. Calibration curve for the ammonium salt of thioxanthonosulfonic acid dioxide on a base electrolyte of 0.2 N KNO₃, constructed from the differential curve.

In buffer solutions the ammonium (sodium) salt of thioxanthonosulfonic acid dioxide also gave well-expressed waves for which the half-wave potential moved toward negative values with an increase in the pH value, while the value of i_d remained constant (Table 2).

* Curve 6 was plotted with the potentiometer moving at a reduced rate and consequently the scale given for this curve equaled 0.1 v.

TABLE 2

Half-wave Potential and Diffusion Current of Ammonium Salt of Thioxanthonosulfonic Acid Dioxide in Buffer Solutions

pH	$E_{1/2}$ (in v)	i_d (in μ a)
2.42	-0.51	19.92
4.58	-0.60	18.72
5.88	-0.65	19.68
6.92	-0.67	20.40
8.95	-0.71	19.44
11.75	-0.78	18.24

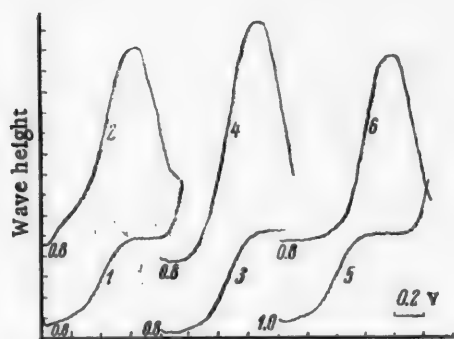


Fig. 3. Integral and differential curves of 3,7-dichlorothioxanthone 5-dioxide on KNO_3 (Curves 1 and 2), KCl (Curves 3 and 4), and NaOH (Curves 5 and 6) base electrolytes.

In hydrochloric acid solutions and acid buffer solutions it was impossible to obtain waves as the hydrogen wave masked that of the main compound. In alkaline buffer solutions the half-wave potential did not change with a change in pH and i_d also remained constant (Table 4).

The diffusion current of the reduction of 3,7-dichlorothioxanthone 5-dioxide was directly proportional to concentration so that it could be used for quantitative determination.

TABLE 3

Half-wave Potentials and Current Maximum Potential of 3,7-Dichlorothioxanthone 5-Dioxide

Base electrolyte	$E_{1/2}$ (in v)	E_{max} (in v)
0.2 N KNO_3	-1.19	-1.45
0.2 N KCl	-1.18	-1.44
0.2 N NaOH	-1.38	-1.56

TABLE 4

Half-wave Potential and Diffusion Current of 3,7-Dichlorothioxanthone 5-Dioxide in Buffer Solutions

pH in the presence of 60% alcohol	$E_{1/2}$ (in v)	i_d (in μ a)
8.5	-1.26	1.32
10.55	-1.26	1.22
12.0	-1.26	1.22

It was also established that the value of the diffusion current of both compounds was proportional to their concentration in solution; quite satisfactory calibration lines were obtained for a KNO_3 base electrolyte and a buffer solution with pH 4.58.

The reduction waves of the ammonium and sodium salts of thioxanthonosulfonic acid dioxide were of the diffusion type since the value of the diffusion current was directly proportional to the square root of the height of the mercury column.

Differential curves were also plotted on the base of the same indifferent electrolytes (Fig. 1); the potential of the peak did not coincide with the half-wave potential, but was slightly (approximately 0.1-0.15 v) displaced in a negative direction, as has also been reported by other authors [5, 6].

The peak heights of the differential curves were directly proportional to concentration. A completely satisfactory calibration line was obtained for the ammonium salt of thioxanthonosulfonic acid dioxide over the concentration range 0.0004 to 0.004 M in a base electrolyte of a 0.2 N solution of KNO_3 (Fig. 2).

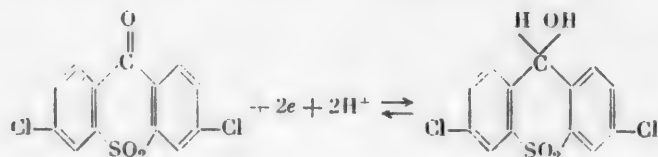
In accordance with the normal polarograms, in a sodium hydroxide base electrolyte two peaks were obtained, which were difficult to separate due to the similarity of their potentials (Fig. 1).

In all the media examined, the reduction of 3,7-dichlorothioxanthone 5-dioxide gave one wave (Fig. 3) with a considerably more negative half-wave potential than for the first two compounds investigated (Table 3).

During the work it was noticed that during polarographic work on all the compounds examined it was necessary to use freshly prepared solutions as these compounds were readily oxidized on standing in air and the reduction waves obtained were distorted.

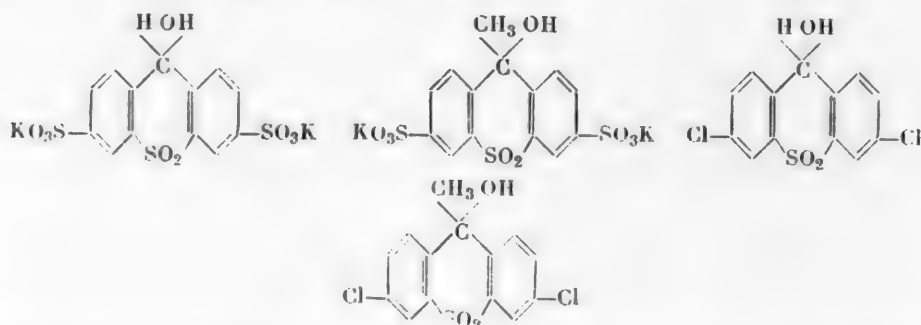
For determining the number of electrons (n) participating in the reduction, we used the microcoulometric method proposed in [7]. As a result of experimental determinations it was found that n for the ammonium and sodium salts of thioxanthonedisulfonic acid dioxide and 3,7-dichlorothioxanthone 5-dioxide equaled about 2.

Hence, we can assume that two electrons participate in the reduction and add according to the scheme:



The reaction for the ammonium and sodium salts of thioxanthonedisulfonic acid dioxide may be written similarly.

This scheme is confirmed by the fact that compounds of similar structure with OH and R groups instead of oxygen (where $R = \text{H}, \text{CH}_3, \text{C}_6\text{H}_5\text{SO}_3\text{K}$), did not give reduction waves when polarographed. Thus, we investigated the reduction of compounds with the following structures:



In the presence of HCl, NaOH, and LiCl solutions none of them were reduced or gave reduction diffusion currents.

SUMMARY

1. The reduction of ammonium and sodium salts of thioxanthonedisulfonic acid dioxide and 3,7-dichlorothioxanthone 5-dioxide on a dropping mercury electrode in various media was investigated.
2. The effect of the pH of the solution on the half-wave potential of the compounds studied was demonstrated.
3. A possible reduction mechanism was proposed on the basis of the calculated value of n .

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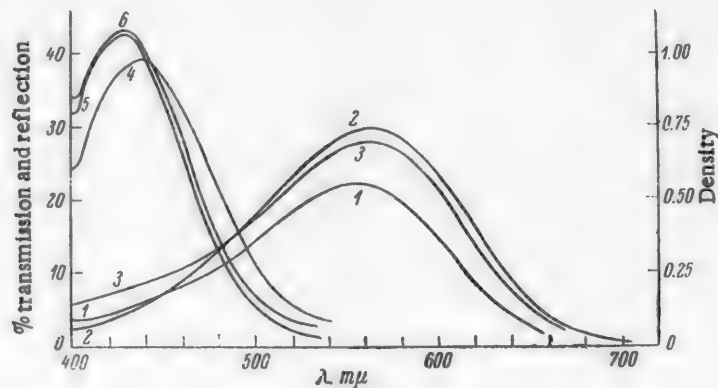
S-BENZYL DERIVATIVES OF ARYLTHIOCARBAZONES

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It was shown that S-benzyl derivatives of diphenylthiocarbazone and o-tolyl- and o-phenoxyphenylthiocarbazones are obtained in *cis-cis*- and *trans-trans*-forms [1].

It seemed interesting to synthesize S-benzyl derivatives of a series of substituted diphenylthiocarbazones under identical conditions and determine the factors affecting the formation of *cis-cis*- or *trans-trans*-forms.



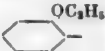

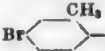




Absorption curves of S-benzyl derivatives in benzene. 1) 1,5-Di-(2-bromophenyl)-thiocarbazone; 2) 1,5-di-(2-methyl-4-bromophenyl)-thiocarbazone; 3) 1,5-di-(4-bromophenyl)-thiocarbazone; 4) 1,5-di-(2-methylmercaptophenyl)-thiocarbazone; 5) 1,5-di-(2-phenetyl)-thiocarbazone; 6) 1,5-di-(2,5-dimethylphenyl)-thiocarbazone.

The benzyl derivatives of aryl thiocarbazones were obtained under the conditions described previously [1]. Alcohol solutions of equimolar amounts of the sodium salts of arylthiocarbazones and benzyl bromide were mixed in the cold. At this, dark violet or orange-yellow crystalline precipitates formed. The precipitates were washed with water, a small amount of alcohol, and ether. The preparations were chromatographed on a column of aluminum oxide and eluted with a mixture of benzene and chloroform. The solvents were removed in vacuum. Nitrogen analysis data confirmed that monobenzyl derivatives were obtained. The absorption curves of the preparations in benzene had one maximum in the region of 555-560 mμ (*trans-trans*-isomer) or in the region of 430-440 mμ (*cis-cis*-isomer) [2]. Evidently, only one isomer was formed under these conditions.

The melting points, yields, absorption maxima, and nitrogen analysis data of the monobenzyl derivatives synthesized are presented in the table.

S-Benzyl Derivatives of Arylthiocarbazonates of the General Formula $\begin{matrix} \text{RNH}-\text{N} \\ \text{RN}=\text{N} \end{matrix} \text{C}=\text{S}-\text{CH}_2\text{C}_6\text{H}_5$

Sam. No.	R	Melting point	Yield (in %)	λ_{max} (m μ)	Empirical formula	Nitrogen (in %)	
						found	calc.
1		163°	65	558	$\text{C}_{22}\text{H}_{22}\text{N}_4\text{S}$	14.64, 14.77	14.95
2		128	68	565	$\text{C}_{24}\text{H}_{20}\text{N}_4\text{S}$	13.95, 13.85	13.93
3		121	72	430	$\text{C}_{24}\text{H}_{20}\text{O}_2\text{N}_4\text{S}$	12.62, 12.74	12.90
4		123	68	565	$\text{C}_{22}\text{H}_{22}\text{N}_4\text{S}_3$	12.61, 12.55	12.78
5		177	83	440	$\text{C}_{22}\text{H}_{20}\text{N}_4\text{SBr}_2$	10.28, 10.35	10.52
6		153	71	430	$\text{C}_{20}\text{H}_{16}\text{N}_4\text{SBr}_2$	10.84, 10.76	11.11
7		129	75	430	$\text{C}_{20}\text{H}_{16}\text{N}_4\text{SBr}_2$	10.86, 10.75	11.11

The figure shows absorption curves of six compounds. The benzyl derivatives of arylthiocarbazonates were orange-yellow or dark violet crystalline compounds. The benzyl derivatives of arylthiocarbazonates with ortho- and para-bromo and ortho-ethoxy substituents formed cis-cis-isomers, while those with methyl (Preparations No. 1 and 2) and ortho-methylmercapto substituents (Preparation No. 4) formed trans-trans-isomers.

SUMMARY

1. Seven S-benzyl derivatives of substituted diphenylthiocarbazonates were synthesized.
2. It was shown that ortho-alkoxy and halo substituted arylthiocarbazonates form yellow cis-cis-isomers, while alkyl and ortho-methylmercapto derivatives form violet trans-trans-isomers.

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S-METHYL DERIVATIVES OF ARYLTHIOCARBAZONES

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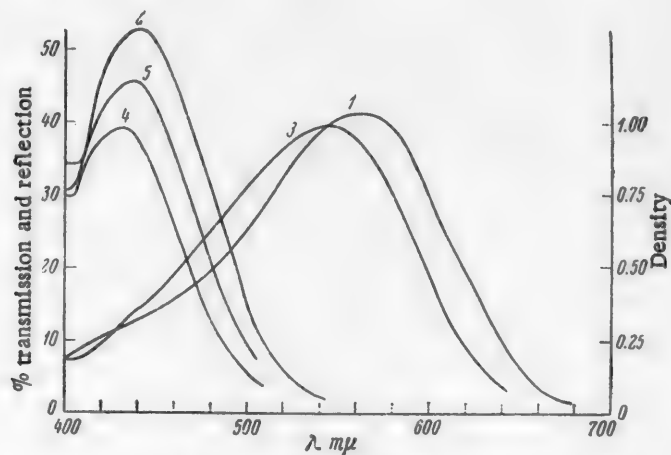
It was previously shown that methylation of substituted 1,5-diphenylthiocarbazonates in an alcoholic alkali solution yielded S-methyl derivatives in *cis*- and *trans*-forms [1-4]. It seemed interesting to determine the nature of the effect of the substituents and their position in the phenyl groups on the formation of *cis*- or *trans*-forms.

S-Methyl Derivatives of Arylthiocarbazonates of the General Formula

$$\begin{array}{c} \text{RNH}-\text{N} \\ \text{R}'\text{N}=\text{N} \end{array} \text{C}=\text{SCH}_3$$

Sample No.	R	R	Melting point	Yield (in %)	λ_{max} , mμ	Empirical formula	found	calc.
1			128°	80	564	C ₁₈ H ₂₂ N ₄ S	17.23, 17.33	17.18
2			115	95	441	C ₁₈ H ₂₂ O ₂ N ₄ S	15.48, 15.70	15.64
3			95	77	578	C ₂₂ H ₃₀ O ₂ N ₄ S	13.21, 13.33	13.52
4			162	88	432	C ₁₄ H ₁₂ N ₄ SI ₂	10.86, 10.92	10.73
5			175	70	432	C ₁₄ H ₁₂ N ₄ SI ₂	10.98, 11.07	10.73
6			168	83	428	C ₁₄ H ₁₂ N ₄ SCI ₂	16.74, 16.86	16.52
7			168	73	437	C ₁₄ H ₁₀ N ₄ SCI ₄	13.91, 13.82	13.72
8			134	76	564	C ₁₆ H ₁₈ N ₄ S	18.48, 18.57	18.79
9			160	96	546	C ₁₈ H ₂₀ O ₂ N ₄ S	15.48, 15.61	15.73
10			144	77	517	C ₁₆ H ₁₇ ON ₄ SCI	15.74, 15.86	16.07

The S-methyl derivatives were synthesized by the method described previously [1, 2]. Equimolecular amounts of arylthiocarbazonates and methyl iodide were mixed in the cold in an alcoholic alkali medium (alkali calculated on the sodium salt of the thiocarbazonate) and the mixture left overnight. The precipitated crystals were collected and washed with a small amount of water, alcohol, and ether. The vacuum-dried substances were chromatographed on columns packed with aluminum oxide [1].



Absorption curves of S-methyl derivatives in benzene. 1) 1,5-Di-(3,4-dimethylphenyl)-thiocarbazonate; 2) 1,5-di-(2-chlorophenyl)-thiocarbazonate; 3) 1-(2-tolyl)-5-(4-carbethoxyphenyl)-thiocarbazonate; 4) 1,5-di-(2-iodophenyl)-thiocarbazonate; 5) 1,5-di-(2,4-dichlorophenyl)-thiocarbazonate.

The melting points, yields, absorption maxima, and nitrogen analysis data of the S-methyl derivatives synthesized are given in the table.

We previously described the synthesis of the starting arylthiocarbazonates for preparations No. 1-7 [5-7]. The starting unsymmetrical arylthiocarbazonates for preparations No. 8-10, which have not been described in the literature, were synthesized according to data in [8].

As the data in the table show, all the preparations had one absorption maximum. The preparations were either yellow-orange or dark violet, crystalline substances and were obtained in good yields.

As has been shown, S-methyl derivatives of arylthiocarbazonates with an absorption maximum at 420-470 cm^{-1} are *cis-cis*-isomers. Compounds with an absorption maximum at 530-570 $\text{m}\mu$ are *trans-trans*-isomers.

The data presented in the table show that 2- and 4-iodo, 2-chloro, 2,4-dichloro, and 2-ethoxy derivatives of 1,5-diphenylthiocarbazonate formed *cis-cis*-isomers; 3,4-dimethyl and 2-n-butoxy derivatives formed *trans-trans*-isomers. Unsymmetrical arylthiocarbazonates formed *trans-trans*-isomers.

The figure shows absorption curves of five S-methyl derivatives. The absorption curves of all the preparations were measured on an SF-2 spectrophotometer for benzene solutions at a concentration of $6.6 \cdot 10^{-5}$ M.

SUMMARY

Ten new S-methyl derivatives of various substituted 1,5-diphenylthiocarbazonates were synthesized and their absorption spectra measured.

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* Original Russian pagination. See C. B. Translation.

UNSYMMETRICAL ORGANIC α -OXIDES

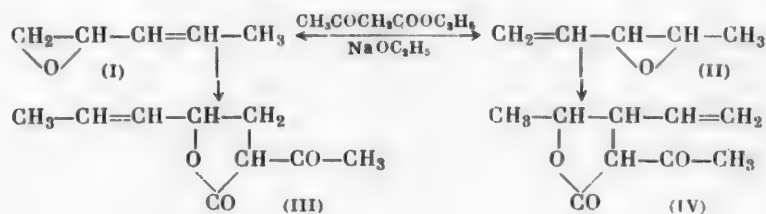
XVIII. CONDENSATION PRODUCTS OF PIPERYLENE OXIDES

WITH SODIOACETOACETIC ESTER AND ACETONE

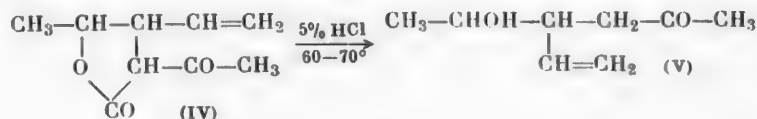
F. G. Ponomarev and N. V. Tinaeva

Voronezh State University

In a previous communication [1], the condensation of 1,2-epoxypentene-3 (I) and 2,3-epoxypentene-4 (II) with sodioacetoacetic ester was described. It was shown that as a result of this reaction, oxide (I) formed mainly α -aceto- γ -propenyl- γ -butyrolactone (III) and oxide (II), α -aceto- β -vinyl- γ -methyl- γ -butyrolactone (IV)*.



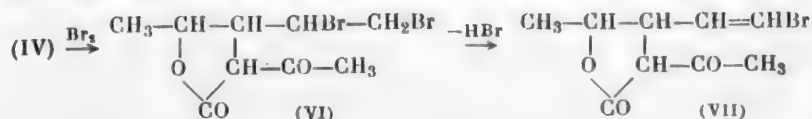
The present work is a continuation of the given investigation. We established that under the action of 5% hydrochloric acid, the unsaturated lactone (IV) was decarboxylated to form the corresponding 5-hydroxy-4-vinylhexanone-2 (V).



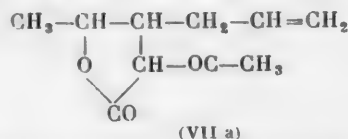
The latter was isolated as the semicarbazone. The unsaturated nature of the keto alcohol obtained and the presence of a hydroxyl group in it were confirmed by the usual reactions for a double bond and an OH group.

* Apart from (III) and (IV), the other possible isomeric lactones (α -aceto- β -propenyl- γ -butyrolactone and α -aceto- β -methyl- γ -vinyl- γ -butyrolactone) were apparently obtained in very small amounts and were not separated by fractionation of the products in vacuum.

** It is possible that the elimination of HBr could also occur in another direction with the formation of the isomer (VIIa). However, this is less probable since the given structure is less stable energetically.

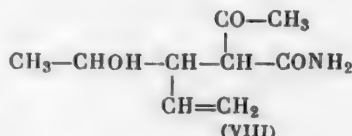


Bromination of the same lactone (IV) in the cold in carbon tetrachloride solution with the calculated amount of bromine yielded not the expected dibromolactone (VI), but a product with a double bond, which according to analysis data and the molecular weight, corresponded to α -aceto- β -(β -bromovinyl)- γ -methyl- γ -butyrolactone (VII). The latter could have been formed by elimination of a hydrogen bromide molecule from the normal bromination product, i.e., the dibromolactone (VI).*

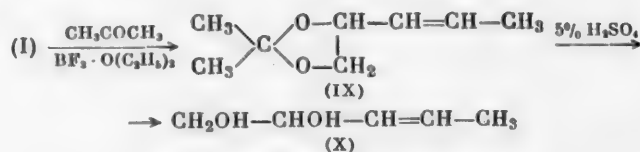


Similar behavior of other dibromolactones (capable of losing hydrogen bromide readily) has also been observed previously [2].

Reaction of lactone (IV) with 25% aqueous ammonia at room temperature formed a substance which had an amide group and, according to analysis data, corresponded to the expected amide of α -aceto- β -vinyl- γ -hydroxyvaleric acid (VIII).



With acetone and under the action of $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$ catalyst, oxide (I) formed 2,2-dimethyl-4-propenyl-dioxolane (IX), whose structure was determined by hydrolysis with 5% H_2SO_4 to form the original acetone and pentene-3-diol-1,2 (X).



EXPERIMENTAL

The starting 1,2-epoxypentene-3 (I) (b. p. 102-104°, n_D^{20} 1.4320) and 2,3-epoxypentene-4 (II) (b. p. 82-84°, n_D^{20} 1.4060) were obtained from piperylene through the halohydrins [3]. α -Aceto- β -vinyl- γ -methyl- γ -butyrolactone (IV) was obtained by heating oxide (II) with sodiumacetoacetic ester in anhydrous alcohol in the presence of sodium ethylate [1] and had b. p. 146-148° (28 mm), n_D^{20} 1.4620, d_4^{20} 1.0592.

Decarboxylation of lactone (IV). To 10 g of lactone (IV) was added 32 ml of 5% hydrochloric acid dropwise and the mixture heated on a water bath at 60-70° for 6 hours (until the evolution of carbon dioxide ceased), then saturated with potassium carbonate and extracted with ether several times; the ether extracts were dried with potassium carbonate. Removal of the ether and vacuum distillation of the residue yielded about 2 g (18.7%) of 5-hydroxy-4-vinylhexanone-2 (V). The keto alcohol (V) was a colorless oil with a pleasant smell. It rapidly decolorized bromine water and potassium permanganate solution. The presence of active hydrogen was demonstrated with metallic sodium and a positive reaction for a ketone group was obtained.

B. p. 106-108° (27 mm), n_D^{20} 1.4502, d_4^{20} 0.9570, M_R 39.76; Calc. 40.21.

Found %: C 67.72; H 10.22. M 140.8, 141.9. $\text{C}_8\text{H}_{14}\text{O}_2$. Calculated %: C 67.61; H 9.86; M 142.22.

Semicarbazone of keto alcohol (V). This compound had m. p. 206-207° (from aqueous alcohol).

Found %: N 25.34. $\text{C}_9\text{H}_{17}\text{O}_2\text{N}_2$. Calculated %: N 25.63.

Bromination of α -aceto- β -vinyl- γ -methyl- γ -butyrolactone (IV). To a solution of 4 g of lactone (IV) in 4 ml of carbon tetrachloride was slowly added 3.5 g of bromine in 70 ml of CCl_4 with cooling (-2°). On the following day the mixture was washed with a saturated aqueous solution of potassium carbonate, then with water and dried with anhydrous sodium sulfate. Removal of the solvent and vacuum distillation of the residue yielded about 1 g of lactone (VII) with a possible trace of (VIIa) as a slightly colored liquid with a sharp smell.

B. p. 160-162° (10 mm), n_D^{20} 1.4920, d_4^{20} 1.3592 MR_D 52.47; Calc. 51.52.

Found %: Br 32.17. M 249.1, 249.4. $C_9H_{11}O_3Br$. Calculated %: Br 32.33. M 247.1.

Ammonolysis of lactone (IV). A mixture of 3 g of lactone (IV) and 22 ml of 25% aqueous ammonia was shaken at room temperature for 30 minutes and then left overnight. The next day the ammonia and water were removed under reduced pressure. The residue, which was a viscous mass, partially crystallized after being dried over $CaCl_2$. The substance was readily soluble in alcohol and chloroform. When it was heated with a 10% aqueous solution of NaOH, the substance gave off ammonia, indicating the presence of an amido group in product (VIII) [4].

Found %: N 9.67. $C_9H_{15}O_3N$. Calculated %: N 9.19.

Condensation of 1,2-epoxypentene-3 (I) with acetone(carried out together with L. D. Bessonova). Under the same conditions as in the reaction of oxide (II) with acetone [3], the reaction of 6.4 g of piperylene oxide (I), 22 g of freshly distilled acetone, and 0.142 g of $BF_3 \cdot O(C_2H_5)_2$ and vacuum distillation of the product in the presence of hydroquinone* yielded 1.2 g (11%) of 2,2-dimethyl-4-propenyldioxolane (IX) as a colorless liquid with a pleasant smell. It was readily soluble in alcohol and ether and sparingly so in water. It rapidly decolorized potassium permanganate solution.

B. p. 23-25° (6 mm), n_D^{20} 1.4215, d_4^{20} 0.9310, MR_D 38.30; Calc. 39.76.

Found %: C 67.50; H 9.82. M 143.4. $C_8H_{14}O_2$. Calculated %: C 67.57; H 9.94. M 144.2

Hydrolysis of dioxolane (IX). Hydrolysis of 2.5 g of dioxolane (IX) with 5% sulfuric acid under the conditions described previously [3] yielded acetone (its semicarbazone, obtained by the usual method, melted at 186-187°) and known pentene-4-diol-1,2 (X) with b. p. 86-87° (10 mm), n_D^{20} 1.4447.

SUMMARY

1. The reactions of α -aceto- β -vinyl- γ -methyl- γ -butyrolactone with 5% hydrochloric acid, bromine, and ammonia were studied. The products of these reactions were obtained and characterized.
2. Condensation of 1,2-epoxypentene-3 with acetone yielded for the first time an unsaturated cyclic ketal, namely, 2,2-dimethyl-4-propenyldioxolane. The structure of the latter was established by its hydrolysis products.

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* Substance (IX) could not be distilled without this stabilizer as it polymerized completely.

** Original Russian pagination. See C. B. Translation.

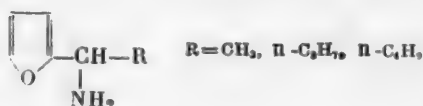
PREPARATION OF α -AMINO ACIDS FROM FURAN DERIVATIVES

II. SYNTHESIS OF ASPARTIC ACID

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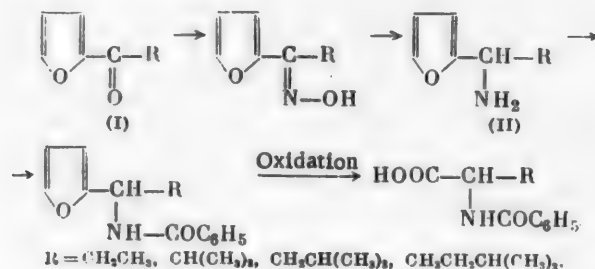
In a previous communication [1] it was shown that benzoyl derivatives of amines of the type



are oxidized by potassium permanganate in an alkaline medium to benzoyl derivatives of amino acids. Three amino acids, namely, alanine, norvaline, and norleucine, were obtained as the benzoyl derivatives in yields of 50-70%.

In the present article we describe the application of this method to the synthesis of benzoyl derivatives of α -aminobutyric acid, leucine, and α -aminoisoeanthic acid.

The general reaction scheme was as follows:



The furyl ketones and their oximes were prepared by the methods given in the previous communication. The oximes were reduced to amines with zinc in acetic acid. The benzoyl derivatives of the amines were oxidized to benzoylamino acids with potassium permanganate in an alkaline medium.

In the case when $\text{R} = \text{CH}(\text{CH}_3)_2$, the oxidation of the benzoyl derivatives of the amine proceeded anomalously. We were unable to isolate benzoylvaline despite variations in the oxidation conditions. In this case the molecule was evidently oxidized more completely and not only the furan ring, but also the tertiary carbon atom was affected. Benzoyl derivatives of amines, containing one or more methylene groups between the carbon atom with the amino group and the tertiary carbon atom, were oxidized normally.

Thus, the method we proposed may be used to prepare amino acids in the form of benzoyl derivatives (with the exception of benzoylvaline).

From the literature it is known that until now amino acids have been prepared from benzoyl derivatives under quite drastic conditions, namely, boiling for six hours with hydrochloric acid [2, 3].

TABLE 1
Furyl Ketones (I)

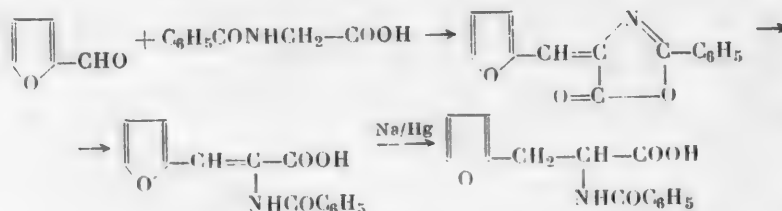
R	Yield (in %)	Boiling point (pressure in mm)		n _D ²⁰	Oxime						
		our data	literature data		our data	literature data	yield (in %)	boiling point (pressure in mm)	empirical formula	N content (in %)	
										found	calc.
CH ₂ CH ₃	57	73—76° (13)	75—80° (12) [8]	—	—	80	102—103° (5) (m.p. 46—47°)	—	—	—	
CH(CH ₃) ₂	60	91—92 (20)	86—87 (18) [9]	1.4885	1.4888	90	121—122 (7)	C ₈ H ₁₁ O ₂ N	9.26, 9.17	9.14	
CH ₂ CH(CH ₃) ₂	60	98—95 (23)	98 (18) [8]	1.4893	1.4891	91	130—132 (7)	C ₉ H ₁₃ O ₂ N	8.47, 8.52	8.38	
CH ₂ CH ₂ CH(CH ₃) ₂	65	115 (20)	119 (22) [8]	1.4842	1.4839	90	144—145 (20)	C ₁₀ H ₁₅ O ₂ N	7.56, 7.84	7.72	

TABLE 2
Furylamines (II)

R	Yield (in %)	Boiling point (pressure in mm)	n _D ²⁰	d ₄ ²⁰	M _R	% C		% H		% N		Benzoyl derivative		
						found	calc.	found	calc.	found	calc.	melting point	empirical formula	found
CH ₂ CH ₃	50	55—56° (7)	1.4770	0.9634	36.71	37.93	—	—	—	—	—	51—52°	—	—
CH(CH ₃) ₂	60	68—69 (9)	1.4730	0.9625	40.57	41.07	—	—	—	10.93, 10.26	10.63	79—80	C ₁₅ H ₁₇ O ₂ N	5.46, 5.52
CH ₂ CH(CH ₃) ₂	62	86—87 (13)	1.4708	0.9462	45.26	45.69	70.41, 70.44	9.95, 9.95	9.87	—	—	70—71	C ₁₆ H ₁₉ O ₂ N	5.53, 5.61
CH ₂ CH ₂ CH(CH ₃) ₂	63	103—105 (15)	1.4705	0.9307	50.23	50.31	71.74, 71.68	10.54, 10.48	10.24	—	—	63—64	C ₁₇ H ₂₁ O ₂ N	5.31, 5.26

In order to develop a more convenient method of isolating amino acids with free amino groups, we oxidized α -furylethylamine in the form of its phthalyl derivative. An advantage of the phthalyl protecting group as compared with the benzoyl was the possibility of isolating free alanine in approximately the same yield (about 50%) without the intermediate isolation of the acyl alanine.

The method described was also applied to the synthesis of dibasic aspartic acid. We prepared this acid by two routes: a) By oxidation of β -(2-furyl)- β -alanine (as the benzoyl derivative), prepared by Rodionov's method from furfural, malonic acid, and ammonium acetate [4]; b) by oxidation of the benzoyl derivative of β -(2-furyl)- α -alanine, synthesized according to the scheme:



Furfurylidenehippuric acid was obtained by Erlenmeyer's method [5]; it was reduced to N-benzoyl- α -furylalanine with 2.5% sodium amalgam [6]. α - and β -N-benzoylfurylalanines were oxidized in aqueous alkali with the theoretical amount of potassium permanganate. The yield of N-benzoylaspartic acid was about 70%. Free aspartic acid was obtained by boiling the benzoyl derivative with dilute hydrochloric acid and precipitation with pyridine [7].

EXPERIMENTAL

Alkyl α -furyl ketones (I). The Grignard reaction was used for the synthesis of ketones [8]. The synthesis of ketones and oximes was described in detail in the previous communication [1].

Amines (II). To a solution of 0.1 mole of alkyl furyl ketone oxime in 100 ml of methyl alcohol was added 25 g of zinc dust. Then acetic acid (50 g) was slowly added dropwise with stirring. The reaction proceeded with evolution of heat and the mixture became slightly yellow. To complete the reaction, the whole mixture was heated for 3 hours on a water bath. The methyl alcohol and acetic acid were removed in vacuum. After the reaction mixture had been made alkaline, the amine was steam distilled. A hydrochloric acid solution of the amine was evaporated to small volume and made alkaline and the amine extracted with ether and dried with alkali. The amine was vacuum distilled with protection from moisture and carbon dioxide (Table 2).

Benzoyl derivatives of α -amino acids. To a solution of 0.01 mole of the benzoyl derivative of the amine in 100 ml of acetone was added 1 ml of 20% potassium hydroxide and then a solution of 8.2 g of potassium permanganate in 250 ml of water, slowly with stirring. The temperature of the reaction mixture was not allowed to rise above 15°. When the solution had become colorless, a further 8.2 g of finely ground potassium permanganate was added and the mixture left overnight. The manganese dioxide was removed by filtration and washed with hot water; the combined filtrates were evaporated to a volume of 25 ml and hydrogen chloride passed into the solution. The precipitated benzoyl derivative was recrystallized from water or dilute alcohol.

N-Benzoyl- α -aminobutyric acid. The yield was 71% and the m. p. 144°. Literature data: m. p. 144° [10].

N-Benzoylleucine. The yield was 75% and the m. p. 138-140° (from alcohol). Literature data: m. p. 137-141° [11].

N-Benzoyl- α -aminoisoeanthic acid. The yield was 70% and the m. p. 133-135°.

Found %: N 5.43, 5.78. $C_{14}H_{19}O_3N$. Calculated %: N 5.61.

1-Phthalimino-1-(α -furyl)-ethane. A mixture of 0.38 mole of α -furylethylamine [1] and 0.38 mole of finely ground phthalic anhydride was heated on an oil bath at 125-130° for 30 minutes. The solid mass was ground with water, filtered, and washed with water. The yield of the phthalyl derivative was 80%; the m. p. was 94-95° (from alcohol). It was insoluble in water and alkali solution.

Found %: C 69.16, 69.61; N 6.07, 6.17, 6.10. $C_{14}H_{11}O_3N$. Calculated %: C 69.70; N 5.81.

α -Alanine. To a solution of 0.018 mole of the phthalyl derivative of α -furylethylamine in 80 ml of acetone was added 1 ml of 40% alkali and then a solution of 17 g of potassium permanganate in 400 ml of water was introduced in small portions with cooling and stirring. After the solution had lost its color, the manganese dioxide was removed by filtration and the filtrate acidified to Congo with hydrochloric acid and boiled for 2 hours. The solution was evaporated to dryness in vacuum. The residue was dissolved in 25 ml of alcohol and 3 ml of pyridine added. The mixture was cooled in an ice bath and the precipitate washed with alcohol and ether. The alanine yield was 46%.

N-Benzoyl- β -(2-furyl)- β -alanine. To a solution of 0.02 mole of β -furylalanine and 1.8 g of potassium hydroxide in 80 ml of water was added 0.034 mole of benzoyl chloride dropwise with cooling and stirring. After 2 hours the mixture was acidified with hydrochloric acid and the precipitate washed with ether. The yield was 80% and the m. p. 179-180° (from water). Literature data: m. p. 179-180° [4].

N-Benzoylaspartic acid. To a mixture of 0.009 mole of N-benzoylfurylalanine and 100 ml of water was added 40% sodium hydroxide solution until solution was complete and then a further 0.5 ml. To the solution obtained was added a solution of 7.4 g of potassium permanganate in 200 ml of water in small portions with cooling and vigorous stirring. After the solution had lost its color, the manganese dioxide was removed by filtration and the filtrate evaporated to small volume in vacuum; hydrogen chloride was passed into the solution. The benzoyl derivative that precipitated on cooling was washed with water. The yield of N-benzoylaspartic acid monohydrate was 74% and the m. p. 116-120°. Recrystallization from water and drying in vacuum at 110° yielded an acid with m. p. 165-166°. Literature data: m. p. 165-166° [12].

Found %: C 55.44, 55.24; N 6.25, 6.20. $C_{11}H_{11}O_5N$. Calculated %: C 55.69; N 5.90.

N-Benzoyl- β -(2-furyl)- α -alanine (0.009 mole) was oxidized analogously. The yield of N-benzoylaspartic acid monohydrate was 60% and the m. p. 116-120°. Literature data: m. p. 119° [7].

Found %: C 51.50, 51.47; N 5.71, 5.82. $C_{11}H_{11}O_5N \cdot H_2O$. Calculated %: C 51.77; N 5.48.

Aspartic acid. A mixture of 0.005 mole of N-benzoylaspartic acid monohydrate, 10 ml of water, and 1 ml of concentrated hydrochloric acid was boiled in a flask for 6 hours. The precipitated crystals of benzoic acid were removed by filtration and the filtrate extracted three times with ether. The aqueous solution was evaporated to dryness, the residue dissolved in 8 ml of alcohol, and 1 ml of pyridine added. The aspartic acid which precipitated on cooling was washed with cold water, alcohol, and ether. The yield was 85% and the compound decomposed above 270°.

Found %: C 36.10, 36.28; N 10.76, 10.99. $C_4H_7O_4N$. Calculated %: C 36.09; N 10.53.

SUMMARY*

By a method proposed previously [1], we synthesized three α -amino acids (as the benzoyl derivatives): α -aminobutyric acid, leucine, and α -aminoisoeanthic acid. α -Furylethylamine was oxidized as the phthalyl derivative. Oxidation of α - and β -N-benzoylfurylalanines yielded aspartic acid.

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* When this work was already complete, we learned that Takahasi [13] also prepared N-benzoylaspartic acid, but by a somewhat different route.

** Original Russian pagination. See C. B. Translation.

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SYNTHESIS AND PROPERTIES OF PYRROLIDINE BASES

VIII. 1-ARYLOXY-3-(2-METHYL-N-PYRROLIDYL)-PROPAN-2-OLS AND SOME OF THEIR DERIVATIVES

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and V. G. Mishina

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In one of our communications [1] we showed that esters of 2-methyl-N- β -hydroxyethylpyrrolidine and some aromatic monobasic acids have physiological activity.

The literature contains reports [2] on the antihistaminic and local anesthetic activity of iodomethylates of some aryloxyalkylpyrrolidones. In 1955, information was published concerning the preparation of some aryloxyhydroxyalkylpyrrolidines [3], but their physiological activity was not examined.

We synthesized a number of 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols and some of their derivatives so as to obtain preparations with possible pharmacological activity.

The method we used for synthesizing pyrrolidine bases by hydroamination of γ -acetopropyl alcohol (I) with formyl derivatives of appropriate amines made it possible to obtain the simplest member of this series, namely, 1-phenoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol, in satisfactory yield (about 50%). However, other pyrrolidine bases of this series were obtained in low yield (10-15%) by hydroamination of γ -acetopropyl alcohol.

To synthesize 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols, we used the method proposed for some 1-aryloxy-3-(N-heterocyclylamino)-propan-2-ols [8]. Condensation of 2-methylpyrrolidine (II) with glycidic ethers of phenols (III) gave 70-85% yields of pyrrolidine bases (IV) (Table 1).

Reaction of 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols (IV) with phenoxyacetyl chloride yielded the corresponding esters (V) (Table 2).

All the conversions mentioned may be represented by the following scheme:

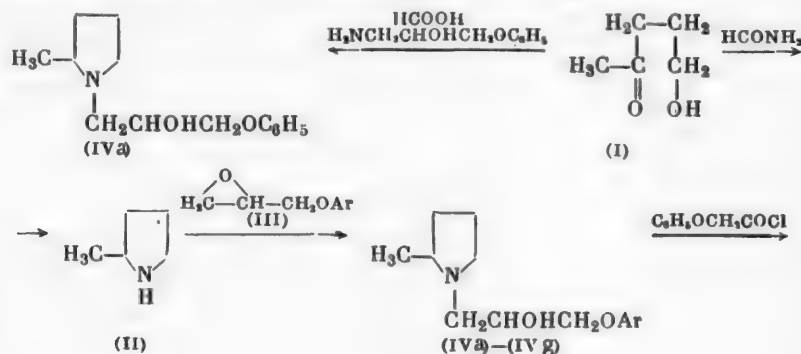
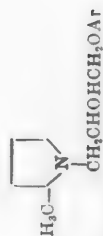
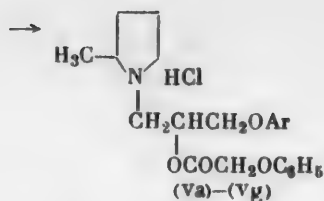


TABLE 1

1-Aryl α - γ -3-(2-methyl-N-pyrrolidyl)-propan-2-ols (IV)

Compound No.	Ar	Boiling point (pressure in mm)	Melting point	Yield (in %)	Hydrochloride					Iodomethylate				
					formula	melting point	found	calc.	% C	% H	found	calc.	% C	% H
(IV a)	Phenyl	153—154 ^a (4)	—	57	$\text{C}_{11}\text{H}_{22}\text{O}_2\text{NCl}$	125°	61.25, 61.38	61.86	8.16, 8.17	—	—	—	—	—
(IV b)	m-Tolyl	156—157 (3)	—	84	$\text{C}_{13}\text{H}_{24}\text{O}_2\text{NCl}$	148—150	—	—	—	—	—	—	—	—
(IV c)	p-Tolyl	160—167 (4)	—	72	$\text{C}_{13}\text{H}_{24}\text{O}_2\text{NCl}$	153—154	—	—	—	5.21, 5.20	—	—	—	—
(IV d)	o-Bromo-phenyl	171—174 (3)	50°	76.3	—	—	—	—	—	—	—	—	—	—
(IV e)	p-Bromo-phenyl	177—180 (3)	45	77.5	—	—	—	—	—	—	—	—	—	—
(IV f)	α -Naphthyl	210—219 (6)	64	75.5	$\text{C}_{18}\text{H}_{24}\text{O}_2\text{NCl}$	153—154	—	—	—	4.70, 4.81	—	—	—	—
(IV g)	α -Naphthyl	208—214 (4)	—	85.3	$\text{C}_{18}\text{H}_{24}\text{O}_2\text{NCl}$	162—163	67.32, 67.47	67.15	—	4.67, 4.50	—	—	—	—



The hydrochlorides and iodomethylates of the 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols synthesized were examined in the Pharmacology Department of the Minsk Medical Institute by I. V. Komissarov. By pharmacological investigation it was found that the hydrochlorides and iodomethylates of 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols had considerable, but short-lived ganglio-blocking and spasmolytic (like papaverine) action with the greater ganglio-blocking effect shown by the iodomethylates and the stronger papaverine-like action shown by the hydrochlorides of these compounds.

EXPERIMENTAL

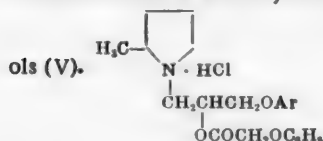
The starting material was technical γ -acetopropyl alcohol, which had the following constants after redistillation:

B. p. 114–115° (30 mm), n_D^{20} 1.4395, d_4^{20} 1.0068, MR_D 26.69.

Literature data [4]: b. p. 115–116° (30 mm), n_D^{20} 1.4390.

TABLE 2

Hydrochlorides of Phenoxyacetates of 1-Aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-



Compound No.	Ar	Formula	Melting point	Yield (in %)	% C		% H		% N	
					found	calc.	found	calc.	found	calc.
(Va)	o-Bromophenyl	$\text{C}_{22}\text{H}_{27}\text{O}_4\text{NClBr}$	190–195°	24.4	54.55, 54.30	54.72	—	—	2.95	2.92
(Vb)	p-Bromophenyl	$\text{C}_{22}\text{H}_{27}\text{O}_4\text{NClBr}$	171–172	24	54.58, 54.40	54.72	—	—	2.94, 2.89	2.92
(Vc)	m-Tolyl	$\text{C}_{23}\text{H}_{30}\text{O}_4\text{NCl}$	132	30	65.72, 65.78	65.78	7.18, 7.14	7.20	—	—
(Vd)	p-Tolyl	$\text{C}_{23}\text{H}_{30}\text{O}_4\text{NCl}$	128	22.8	65.92, 65.96	67.78	7.28, 7.34	7.20	—	—
(Ve)	α -Naphthyl	$\text{C}_{26}\text{H}_{30}\text{O}_4\text{NCl}$	186	20	68.49, 68.27	68.88	6.54, 6.48	6.63	—	—
(Vf)	β -Naphthyl	$\text{C}_{26}\text{H}_{30}\text{O}_4\text{NCl}$	173	20.2	68.38, 68.33	68.88	6.57, 6.51	6.63	—	—

2-Methylpyrrolidine was obtained by hydroamination of γ -acetopropyl alcohol as we described previously [5]. From 40.8 g of γ -acetopropyl alcohol we obtained 11 g (32%) of 2-methylpyrrolidine with b. p. 97–99° (744 mm) and n_D^{20} 1.4340.

Glycidic ethers of phenols. Glycidic ethers of phenol, m-cresol, p-bromophenol, and α -naphthol were obtained by heating a mixture of phenol and dichlorohydrin in the presence of sodium hydroxide [6]. Glycidic ethers of o-bromophenol, p-cresol, and β -naphthol were prepared by condensation of the appropriate phenol with epichlorohydrin in the presence of piperidine and subsequent elimination of hydrogen chloride from the 1-aryloxy-3-chloropropan-2-ols formed [7].

TABLE 3

Glycidic Ethers of Phenols (III) $\text{H}_2\text{C}-\text{CH}-\text{CH}_2\text{OAr}$ 

Compound No.	Ar	Formula	Boiling point (pressure in mm)	melting point	n_D^{20}	d_4^{20}	$M R_D$		yield (%)
							calc.	found	
(IIIa)	Phenyl [6]	$\text{C}_9\text{H}_{10}\text{O}_2$	112° (8)	—	1.5318	1.1113	41.96	41.8	45
(IIIb)	m-Tolyl [8]	$\text{C}_{10}\text{H}_{12}\text{O}_2$	122—123 (8)	—	1.5270	1.0801	46.58	46.74	42
(IIIc)	p-Tolyl [9]	$\text{C}_{10}\text{H}_{12}\text{O}_2$	119—121 (7)	—	1.5268	1.0794	46.58	46.75	—
(IIId)	p-Bromophenyl [10]	$\text{C}_9\text{H}_9\text{O}_2\text{Br}$	135—137 (4)	52°	—	—	—	—	42
(IIIe)	o-Bromophenyl	$\text{C}_9\text{H}_9\text{O}_2\text{Br}$	131 (3)	—	1.5702	1.5174	49.22	49.56	—
(IIIf)	α -Naphthyl [11]	$\text{C}_{13}\text{H}_{12}\text{O}_2$	148—150 (2)	—	1.6097	1.1624	57.30	57.70	45
(IIIg)	β -Naphthyl [12]	$\text{C}_{13}\text{H}_{12}\text{O}_2$	158—159 (3)	81	—	—	—	—	—

1-Phenoxy-3-aminopropan-2-ol. To a saturated solution (in the cold) of 65 g of ammonia in 300 ml of anhydrous methanol was added 50 g of glycidic ether of phenol in 50 ml of anhydrous methanol. The reaction mixture was kept in an ampoule for three days. Removal of the solvent left an oil which rapidly crystallized on cooling. We obtained 53 g (95%) of 1-phenoxy-3-aminopropan-2-ol. The m. p. was 97°. Literature data [13]: m. p. 97–98°.

Hydrochloride: m. p. 136°. Literature data [13]: m. p. 136°.

Found %: C 52.89, 52.95; H 6.85, 6.82. $\text{C}_9\text{H}_{14}\text{O}_2\text{NCl}$. Calculated %: C 53.07.

1-Phenoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol (IVa). A mixture of 15.3 g of γ -acetopropyl alcohol, 52.8 g of 1-phenoxy-3-aminopropan-2-ol, 21 ml of 85% formic acid, and 1.5 g of nickel (from nickel formate) was heated until the evolution of carbon dioxide ceased with distillation of water. After 12 hours, carbon dioxide liberation slowed and then 20 ml of formic acid was added and heating continued for 20 hours with a gradual increase in temperature to 180°. The reaction mixture was hydrolyzed by boiling with 150 ml of concentrated hydrochloric acid for 2 hours, neutralized with 40% sodium hydroxide solution, and extracted with ether. The oil remaining after removal of the ether was fractionated in vacuum. We obtained 16.7 g (47.5%) of 1-phenoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol. The b. p. was 165–170° (8 mm).

1- β -Naphthoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol (IVg). Glycidic ether of β -naphthol (8.5 g) was added in small portions with vigorous stirring to boiling 2-methylpyrrolidine (3.4 g) over a period of 30 minutes. After being heated for 2 hours at 142–149° with stirring, the reaction mixture was fractionated in vacuum. We obtained 8.95 g (85.3%) of 1- β -naphthoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol. B. p. 208–214° at 4 mm.

Hydrochloride of phenoxyacetate of 1- β -naphthoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol. (Vf). A solution of 1.43 g of phenoxyacetyl chloride in 6 ml of absolute ether was added dropwise over a period of 30 minutes with vigorous stirring and cooling to a solution of 1.6 g of 1- β -naphthoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol in 10 ml of absolute ether. A white, crystalline precipitate appeared very rapidly and this was collected and washed on the filter with absolute ether. Recrystallization yielded 0.5 g (20.2%) of the hydrochloride of the phenoxyacetate of 1- β -naphthoxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol. The m. p. was 173°.

The phenoxyacetates of the 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ol were obtained analogously. Toluene could not be used as the solvent.

SUMMARY

1. Condensation of 2-methylpyrrolidine with glycidic ethers of phenols yielded six 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols.

2. Reaction of 1-aryloxy-3-(2-methyl-N-pyrrolidyl)-propan-2-ols with phenoxyacetyl chloride yielded phenoxyacetates of the corresponding pyrrolidine bases, which were isolated as the hydrochlorides.

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INVESTIGATION OF THE PROPERTIES OF AMINO ACIDS AND PEPTIDES CONTAINING A TERTIARY NITROGEN ATOM

I. SIMULTANEOUS DECARBOXYLATION AND DEAMINATION OF N, N-DIBENZYL- α -AMINO ACID CHLORIDES

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The problem of the effect of protective groups on the properties of amino acids and peptides has been little studied and there are only a small number of disconnected facts in the literature. For example, it is known that there is a protective effect in carbobenzoxyamino acids which is expressed in the ease of formation of Leuchs anhydrides from the acid chlorides [1] and in the formation of hydantoins by the cyclization of some carbobenzoxytripeptides [2]. The phthalyl protective effect is also known, which is shown in the increased stability of the phthalylamino acid chlorides. Of interest in this connection are the recent investigations of A. Beecham [3], who established that N-tosyl- α -amino acid chlorides decompose in aqueous alkali with the formation of toluenesulfonamide, aldehyde, and carbon monoxide.

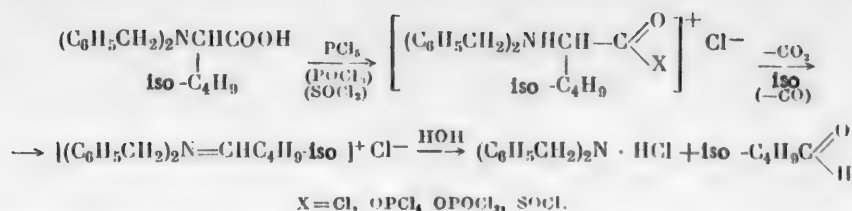
The dibenzyl protection suggested by Velluz et al., [4-7], in 1954 differs from the previously well investigated protective effects (mainly acyl) in that in this case there is a tertiary nitrogen atom in the molecule. Furthermore, the two benzyl groups because of their nucleophilic nature may exert a specific influence on the chemical properties of the amino acids and peptides.

Use of the carbobenzoxyamino acid chlorides for aminoacylation is impossible because of their decomposition with the formation of Leuchs anhydrides [1] and polymerization of the latter. It has been assumed that the dibenzylamino acids do not have this drawback, and all the more so since the dibenzylamino acid chlorides had already been suggested by Velluz et al. [4] for the synthesis of α -benzylpeptides. Indicating the possibility of this synthesis for all amino acids, the authors reported only syntheses with dibenzylglycine and prepared by this method only two compounds: N,N-dibenzylglycylglycine and N,N-dibenzyltriglycine.

We have used this method for the preparation of N,N-dibenzylleucine chloride with the purpose of utilizing it subsequently in a peptide synthesis and for aminoacylation of diketopiperazines. A solution of N,N-dibenzylleucine in an organic solvent was treated with phosphorus pentachloride. Even in the cold, partial decarboxylation of the N,N-dibenzylleucine chloride took place (vigorous evolution of CO₂ and HCl). We were not able to use the precipitate that separated out (supposedly N,N-dibenzylleucine chloride) for the acylation of alcohol and the Na salt of the amino acid. Instead of acylation, decomposition of the N,N-dibenzylleucine was observed, with the formation of dibenzylamine hydrochloride (95% yield) and isovaleraldehyde (77% yield). The latter was identified as its 2,4-dinitrophenylhydrazone.

N,N-Dibenzylleucine chloride also decomposed in boiling xylene extremely rapidly with vigorous evolution of gas, tar formation, and the production of crystalline dibenzylamine hydrochloride, as a result of which it could not be used for the aminoacylation of diketopiperazines, which requires a high temperature (140-160°).

The first stage of the decomposition evidently is a decarboxylation; dibenzylamine hydrochloride appears only after the addition of water. We have assumed that the reaction proceeds according to the following scheme:

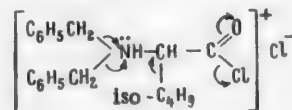


Since CO₂ was collected in carrying out the reaction, its appearance may be explained by the formation of mixed anhydrides with phosphorus compounds.

Decarboxylation proceeds smoothly at 20°, slows down at 0°, and goes extremely vigorously at 50° and above. Decomposition with the formation of dibenzylamine hydrochloride is observed also as a result of the action of phosphorus oxychloride and thionyl chloride. It should be noted that apparently at the moment of the action of phosphorus pentachloride (or POCl₃ and SOCl₂) a more extensive change takes place than simple formation of the acid chlorides.

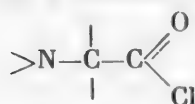
Under the reaction conditions an atom of nitrogen is ammoniated and acquires a positive charge. In this case decomposition of N,N-dibenzylleucine chloride can be compared with the decomposition, for example, of nitroacetic acid. Then it becomes inexplicable that the hydrochloride of N,N-methylbenzylglycine chloride, according to the data of Mannich and Kuphal [8], does not decompose in boiling nitrobenzene and N,N-methylbenzylglycine can be recovered from it.

If the hydrochloride of the acid chloride is formed (as has already been mentioned, mixed anhydrides also can be formed with PCl₄, POCl₂, and SOCl groups), then the effect of various substituents on the nitrogen and carbon produces an increase in electron density on the nitrogen and a strong discharge of the electron density on the carbonyl carbon.



The same holds true if a mixed anhydride is formed instead of an acid chloride.

In this case apparently a phenomenon will occur similar to that which was observed in the investigation by A. Beecham already mentioned, in which he studied the decomposition of N-tosyl-α-amino acid chlorides [3]. A Beecham viewed this reaction as caused mainly by the shift of electrons in the system

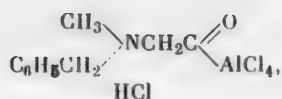


Concentration of the electron density at the nitrogen and its discharge from the carbonyl

carbon leads to a situation where the electron pair forming the C-C bond shifts completely to the carbonyl carbon (the C-C bond ruptures and the oxygen is decarboxylated) and the electron pair on the nitrogen is drawn to the remaining carbon atom (a second bond is formed between the nitrogen and the carbon). As a result, the acid chloride breaks down into tosyl amide and aldehyde. An analogy exists here with the peculiar behavior of the glycine derivatives. We have noted (qualitatively by electrophoresis on paper) only partial decomposition of N,N-dibenzylglycine chloride in 20-30 minutes in the presence of moisture and complete decomposition upon boiling in benzene.

In confirmation of the electron mechanism we can cite the data of Mannich and Kuphal [8], who described as mentioned above, the stability of the hydrochlorides of N,N-methylbenzylglycine chloride in boiling nitrobenzene and its breakdown in the same solvent upon heating with aluminum chloride. In comparison with N,N-dibenzylglycine, the N,N-methylbenzylglycine appeared more stable.

Upon reaction with aluminum chloride, apparently, an intermediate compound of the following type is formed



which results in instability of the molecule and explains the ease of its decomposition.

It may be anticipated that the acid chlorides of the N,N-dibenzyleptides will prove to be more stable and suitable for aminoacylation. In this case the dibenzyl group is further removed from the carboxyl and its effect on the carboxyl is weakened. Investigation of the properties of the acid halides of the N,N-dibenzylamino acids and peptides and the possibility of using them for aminoacylation is being continued. On the basis of the preliminary experimental data it can be said that phosphorus pentachloride does not cause decarboxylation of N,N-dibenzyleptides, even when heated; at the end of the experiment it is possible to regenerate the unchanged peptide.

Solvent		Amount of reagents (in moles)		Temperature		Yield of hydrochloride of dibenzylleucine chloride	
method of drying	amount (in ml)	dibenzyl- leucine	phospho- rus pen- tachloride	initial	final	(in g)	in %
Benzene, washed w. conc. H ₂ SO ₄ and distilled over sodium	4	0.05	0.087	room		0.7	38
	2	0.03	0.058	room		0.4	34
Benzene, washed w. conc. H ₂ SO ₄ , distilled twice over P ₂ O ₅ and once over sodium	10	0.09	0.135	0°	50°	2.1	64
	8	0.13	0.22	0	50	3.8	79
	6	0.08	0.135	0	80	1.1	37
	5	0.05	0.05	50	50	0	0
Ether (absolute)	10	0.03	0.058	room		0	0

EXPERIMENTAL

Preparation of N,N-dibenzylleucine [6].* 6.55 g of leucine was mixed with 100 ml of 50% alcohol and 30 ml of 7 N sodium hydroxide solution. 25 ml of benzyl chloride was added to the boiling mixture in the course of 10-12 minutes. The mixture was heated for 1.5 hours. The solution was evaporated in vacuo and the residue was extracted with carbon tetrachloride. The extract was filtered, washed with water, and the carbon tetrachloride was distilled off in vacuo. To the oil that was formed was added 40 ml of 20% NaOH solution in 20% aqueous glycerin, and the mixture was boiled for 15 minutes. After the hydrolysis, the oil was separated off and, following the addition to it of a solution of 7 g of NaOH in 10 ml of water, it was steam distilled for 2-3 hours, until the distillate became clear. The residue in the flask was acidified with glacial acetic acid and extracted with carbon tetrachloride, the extract was dried, and the solvent was distilled off in vacuo. Upon standing in the cold, the material crystallized. The crystals were separated by suction and washed with petroleum ether. Yield 8.6 g (57%). M. p. 101-102°. According to the literature data, m. p. 99° [7] and 104-106° [6]. The compound was soluble in all organic solvents, though only slightly so in petroleum ether and cyclohexane, and was soluble to a negligible extent in sodium carbonate and alkali solutions and completely insoluble in water and hydrochloric acid.

For N,N-dibenzylleucine in butanol saturated with water and in the system butanol-water-acetic acid (4:5:1) we found the values R_f 0.92 and 0.95, respectively. The compound was developed on the chromatogram with benzidine by the method of Reindel and Hoppe.

* We modified the method of [6] by using milder conditions of hydrolysis and steam distilling off the benzyl alcohol that was formed.

Preparation of the hydrochloride of N,N-dibenzylleucine chloride. N,N-Dibenzylleucine was dried for several hours in a Fisher pistol at 80° and then reacted with phosphorus pentachloride in different solvents and in different proportions. The results of the experiments are given in the table.

To a solution of N,N-dibenzylleucine in a chlorinator, N. I. Gavrilov added phosphorus pentachloride. Depending on the temperature, a more or less vigorous evolution of gas and heat was observed. The precipitate that formed after some time was filtered off, and washed with petroleum ether. A white, crystalline, extremely hygroscopic material was obtained with an indefinite melting point (about 90° with decomp.), insoluble in benzene, xylene, chloroform, carbon tetrachloride, and ether, but soluble in dioxane and especially in acetone; from the last solvent dibenzylamine hydrochloride precipitated upon the addition of water as white lamellar crystals.

Investigation of decomposition. a) Isolation of dibenzylamine hydrochloride. To 2 g of phosphorus pentachloride were added 15 ml of absolute ether and 2 g of N,N-dibenzylleucine in 15 ml of ether, with cooling to 0°. When the temperature was increased to that of the room, a strong evolution of gas began (baryta water became turbid). When the evolution of gas ceased, ether was repeatedly distilled off in vacuo to more completely remove the POCl₃ and HCl. The crystalline precipitate was filtered off, washed with acetone, and dried in a Fisher pistol over toluene. Yield 1.5 g (95%), m. p. 255° (in sealed capillary). Literature data: M. p. 255-256° [9].

Found %: C 71.70, 71.84; H 7.03, 6.98. C₁₄H₁₈NCl. Calculated %: C 71.95; H 6.85.

By the same method, dibenzylamine hydrochloride was isolated from N,N-dibenzylleucine when the latter was reacted with phosphorus oxychloride and thionyl chloride. Material was obtained with the same melting point (255°). A mixed melting point showed no depression.

b) Isolation of 2,4-dinitrophenylhydrazone of isovaleraldehyde. 3.1 g of N,N-dibenzylleucine in 50 ml of absolute ether was treated with 3.0 g of phosphorus pentachloride at 20-30°. After the evolution of gas had ceased, 50 ml of water was added and the mixture was left overnight. The dibenzylamine hydrochloride was filtered off. The ether layer was separated off and the ether was evaporated almost completely. The aldehyde was dissolved in 10 ml of alcohol and to it was added a solution of 2,4-dinitrophenylhydrazine in alcohol (0.5 g of 2,4-dinitrophenylhydrazine was dissolved in 2 ml of conc. H₂SO₄, 3 ml of water, and 10 ml of alcohol). The mixture was heated to boiling for several minutes. Upon cooling, a precipitate separated. Yield 2 g (77%). The material was recrystallized twice from 70% alcohol. M. P. 121-122°. Literature data: M. p. 123° [10].

Isolation of dibenzylamine hydrochloride on reaction of PCl₅ with N,N-dibenzylglycine. To a boiling mixture of 15 ml of anhydrous benzene and 1.1 g of phosphorus pentachloride was added 1.3 g of N,N-dibenzylglycine. Heating was continued for 1.5-2 hours. After cooling, twice the volume of ether was added to the reaction mixture. A semisolid oil separated, which crystallized after being treated with acetone. The crystals were filtered off, carefully washed with acetone, recrystallized from chloroform, and dried in a Fisher pistol over toluene. M. p. 255° (with decomp., in a sealed capillary). A mixed sample with dibenzylamine hydrochloride melted at 254° (with much tar formation). The identity of these materials was confirmed by electrochromatographing on paper. The yield of dibenzylamine hydrochloride was low (10-15%).

Decomposition of N,N-dibenzylleucine chloride in boiling xylene. About 2 g of solid N,N-dibenzylleucine chloride was introduced in portions into boiling anhydrous xylene. When this was done, vigorous evolution of gas, tar formation, and the formation of a crystalline precipitate were observed. The mixture was cooled and absolute ether was added. The crystals were filtered off and washed with acetone. M. p. 250°. Yield about 40% (calculated on the acid chloride). Electrophoresis on paper confirmed the identity of this material with dibenzylamine hydrochloride.

SUMMARY

1. The decomposition of N,N-dibenzylleucine chloride has been investigated. The reaction products have been isolated and a scheme has been proposed for the decomposition of N,N-dibenzylleucine chloride.

2. It has been shown through the example of N,N-dibenzylleucine that the acid chlorides of dibenzylamino acids can not be used for aminoacylation.

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** Russian translation.

THE MECHANISM OF THE CONVERSION OF α -ACYLAMIDO- β -HYDROXYPROPIOPHENONES TO THE CORRESPONDING BENZOYLACETYL

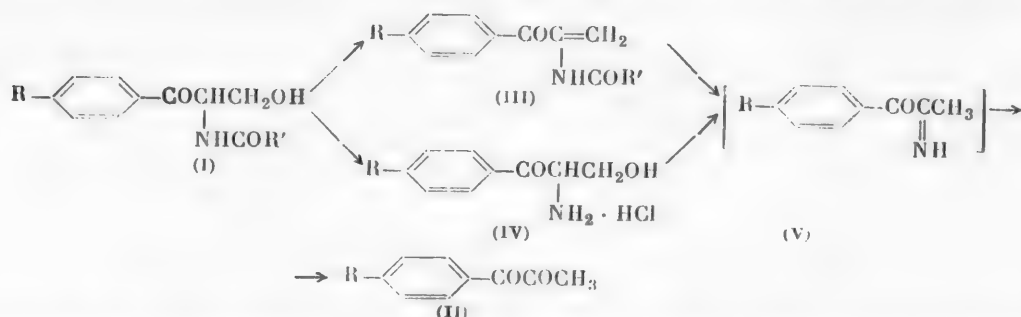
I. SYNTHESIS AND CLEAVAGE OF α -BENZENESULFONAMIDO- AND α -BENZENESULFOMETHYLAMIDO- β -HYDROXYPROPIOPHENONES

V. A. Mikhalev, M. I. Dorokhova, and N. E. Smolina

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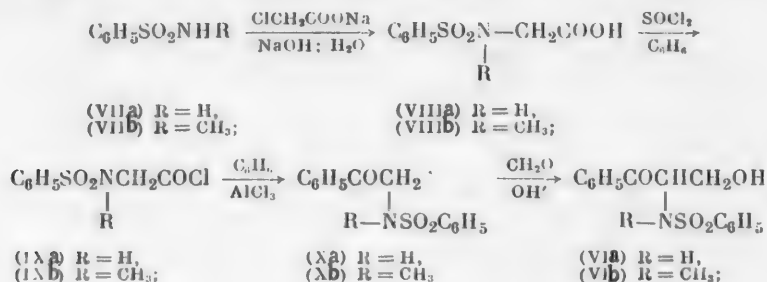
In an investigation of the properties of α -acylamido- β -hydroxypropiophenones (I) it was discovered that these compounds, either unsubstituted or with various substituents in the para position of the benzene ring, are cleaved upon heating with aqueous solutions of mineral acids to form the corresponding benzoylacetyls (II) [1-3]. It was shown that α -acetamido- β -hydroxypropiophenones (I) are converted by different influences to α -acylamidoacrylophenones (III), which also form benzoylacetyls (II) [1,3] upon heating with aqueous solutions of mineral acids. When p-nitro- α -acetamido- β -hydroxypropiophenone was reacted with hydrochloric acid [1,3], it was possible to isolate also the normal hydrolysis product, p-nitro- α -amino- β -hydroxypropiophenone. The latter was converted by prolonged heating with hydrochloric acid to p-nitrobenzoylacetyl.

On the basis of the investigations described it was possible to assume that the conversion of (I) to (II) by the action of mineral acids proceeds by two routes: 1) As a result of the hydrolysis of the acylamido group, salts of the corresponding α -amino- β -hydroxypropiophenone (IV) are formed; 2) splitting out of water takes place initially, with the formation of α -acylamidoacrylophenones (III). Compounds (III) and (IV), upon further heating, split out an acyl radical or a molecule of water and are converted to the same monoimine of the corresponding benzoylacetyl (V), which decomposes in mineral acid medium to the free diketone (II) and the ammonium salt.

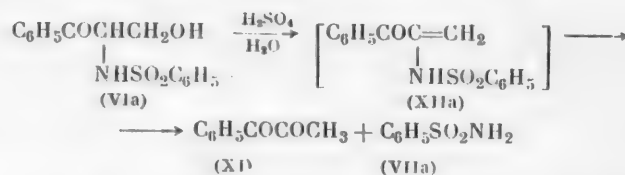


However, the experimental data, and primarily the experiments of Petrov and co-authors, who carried out the conversion of (I) to (II) also by heating with 80% formic acid [1], in the presence of which dehydration readily occurs, but hydrolysis of the acylamido groups does not usually take place, yielded indirect evidence of the possibility of direct hydrolysis of the nitrogen-carbon bond in the acylamidoacrylophenones (III) with splitting out of the acylamide and direct formation of the benzoylacetyls (II). The discovery of the free acylamide among the reaction products would serve as direct evidence of such a course for the process. Transition from the acylamides to the sulfonamides could facilitate the solution of the problem as a result of the greater stability of the sulfonamide bond under the conditions of acid hydrolysis.

It was decided to synthesize α -benzenesulfonamido- β -hydroxypropiophenone (VIa) and to investigate the possibility of converting it to benzoylacetyl. The synthesis was accomplished with about 60% yield of (VIa) calculated on the starting sulfonamide (VIIa) according to the scheme:



The α -benzenesulfonamido- β -hydroxypropiophenone (VIa) obtained was broken down by boiling with 40% sulfuric acid to form benzoylacetyl (XI) and the starting sulfonamide (VIIa).



The yield of (XI) was about 90%. Thus, it was shown that hydrolysis of the acyl group is not an obligatory step in the conversion of (I) to (II).

In order to exclude the possibility of conversion of the amino group to an imino group in the hypothetical intermediate product (XIIa) by analogy with the scheme shown above, we prepared from the sodium salt of benzenesulfomethylamide the α -benzenesulfomethylamido- β -hydroxypropiophenone (VIb), which was cleaved, like (VIa), upon boiling with 40% sulfuric acid to benzoylacetyl (XI) and benzenesulfomethylamide (VIIb).

From what has been stated it is sufficiently obvious that the conversion of α -acylamido- β -hydroxypropiophenones to benzoylacetyls can proceed through the hydrolysis of the simple nitrogen-carbon bond. The formation of the free amino compounds (IV) and (V) is not an obligatory step in the reaction and is observed in those instances where the acyl group is readily hydrolyzed. It is most probable to suppose that an intermediate step of such a conversion is the formation of acylamidoacrylophenones. The lack of success that has attended attempts to isolate these still hypothetical intermediate compounds directly from the reaction medium can be explained by the fact that their rate of conversion to the benzoylacetyls greatly exceeds the rate at which they are formed.

EXPERIMENTAL

Benzenesulfonamidoacetic acid (VIIIa). To a solution of 353 g of benzenesulfonamide* in a mixture of 720 ml of water and 244 ml of 42% sodium hydroxide, heated to 90-95°, was added at once a solution of 142 g of monochloroacetic acid in 210 ml of water. The mixture was kept 3 hours at 90-95°, acidified to pH 6-7, cooled to 25-30°, kept at that temperature for 1-2 hours, and the unreacted benzenesulfonamide (140.8 g) was filtered off. The filtrate was acidified to pH 2-2.5, left overnight, and then the crystals that had precipitated were filtered off and dried. 252 g of benzenesulfonamidoacetic acid was obtained with m. p. 160-163°. After recrystallization from aqueous methanol, it melted at 165-166°, in agreement with the literature data [4].

If the filtrate from (VIIIa) was acidified to pH 1, then on standing for 1-2 days there settled out from it 1-2 g of benzenesulfonimidodiacetic acid in long needles with m. p. 188.5-190°.

* In preparing (VIIIa) it is necessary to introduce into the reaction a considerable excess of benzenesulfonamide. When the amount of benzenesulfonamide is decreased, the amount of by-product benzenesulfonimidodiacetic acid is increased.

Found %: N 4.93, 5.28. $C_{10}H_{11}O_8NS$. Calculated %: N 5.13.

Benzenesulfomethylamidoacetic acid (VIIIb). 94.5 g of monochloroacetic acid was dissolved in 250 ml of water. The solution was neutralized with dry sodium carbonate and divided into two equal portions. The first half was immediately mixed with a solution of 100.1 g of sodium salt of benzenesulfomethylamide in 125 ml of water heated to boiling. The mixture was kept for 1 hour at 90-95°, then the second half of the solution was added and the same temperature was maintained for 1 hour. During this whole process the presence of an alkaline reaction was checked periodically with thymophthalein and 40% sodium hydroxide solution was added as needed. Upon cooling, the solution was acidified with hydrochloric acid to pH 1-1.5, and the precipitate that separated out was filtered off and dried. 99.8 g of benzenesulfomethylamidoacetic acid was obtained, with m. p. 179.5-180.5°; according to the literature [5], m. p. 179°.

Benzenesulfomethylamidoacetyl chloride (IXb). In a flask fitted with a stirrer and reflux condenser were placed 22.9 g of (VIIIb), 140 ml of benzene, 12.4 g of thionyl chloride, and 0.4 ml of pyridine. The reaction mixture was stirred at 45-55° until the evolution of hydrogen chloride ceased (2-3 hours), the benzene was distilled off in vacuo, and the residue was recrystallized from a mixture of benzene and petroleum ether. The compound formed colorless prisms, poorly soluble in petroleum ether, readily soluble in benzene, chloroform, and ether. M. p. 41-42°.

Found %: Cl 14.20, 13.97. $C_9H_{10}O_3NSCl$. Calculated %: Cl 14.39.

Benzenesulfonamidoacetyl chloride (IXa) was prepared in a similar manner to the preceding. The compound after recrystallization from benzene formed colorless needles with m. p. 87.5-88.5°.

Found %: Cl 14.65, 14.75; N 6.16. $C_8H_8O_3NSCl$. Calculated %: Cl 15.20; N 6.0.

α -Benzenesulfomethylamidoacetophenone (Xb). In a flask fitted with a stirrer, thermometer, dropping funnel, and reflux condenser were placed 23 g of anhydrous aluminum chloride and 85 ml of benzene, and then, while stirring was continued at 10-20°, a benzene solution of benzenesulfomethylamidoacetyl chloride prepared from 22.9 g of (VIIIb) was added from the dropping funnel over a period of 10-15 minutes. The reaction mixture was stirred for 2 hours at 25-30°, cooled to 10°, and a solution of 10 ml of concentrated hydrochloric acid in 100 ml of water was added to it at such a rate that the temperature did not rise above 40°. The warm benzene layer was separated, the benzene was steam-distilled off, and the residue, after separation from the water, was recrystallized from alcohol.

23.9 g (82.8% calculated on VIIIb) of compound was obtained, which formed colorless prisms with m. p. 111-112°.

Found %: C 62.27; H 5.26; N 4.95, 4.70; S 11.14. $C_{15}H_{15}O_3NS$. Calculated %: C 62.27; H 5.23; N 4.84; S 11.08.

α -Benzenesulfonamidoacetophenone (Xa) was prepared in a similar manner to the preceding, but after the addition of hydrochloric acid the mixture was left overnight, then the crystals that precipitated were filtered off and washed with water until there was no acid reaction to Congo. After recrystallization from alcohol the compound formed colorless needles with m. p. 142-143°.

Found %: C 60.87; H 4.71; N 5.22. $C_{14}H_{13}O_3NS$. Calculated %: C 61.07; H 4.76; N 5.09.

α -Benzenesulfonamido- β -hydroxypropiofenone (VIa). 137.5 g of (Xa), 580 ml of 50% isopropyl alcohol, 69 ml of 40% formalin, and 13.8 g of sodium bicarbonate were stirred for 40 minutes at 59-60°. The reaction mixture was cooled to 15° and filtered. The precipitate was washed with water, 5% hydrochloric acid, and water again. 119 g (78.0%) of α -benzenesulfonamido- β -hydroxypropiofenone was obtained with m. p. 138.5-139.5°. After recrystallization from alcohol the compound formed colorless plates with m. p. 139-140.5°.

Found %: C 59.00; H 5.17; N 4.64, 4.65. $C_{15}H_{15}O_4NS$. Calculated %: C 59.01; H 4.95; N 4.59.

α -Benzenesulfomethylamido- β -hydroxypropiofenone (VIb). 5.8 g of (Xb), 29 ml of 50% alcohol, 2.8 ml of 40% formalin, and 1.7 ml of 20% sodium hydroxide were quickly heated to 70° and stirred at this temperature for 30-40 minutes, cooled to 50°, stirred for another 1.5 hours, and cooled to room temperature. The precipitate was filtered off and washed with water and alcohol. 4.27 g (66.8%) of α -benzenesulfomethylamido- β -hydroxypropiofenone with m. p. 121-123° was obtained. After recrystallization from alcohol the compound was obtained as colorless platelets with m. p. 123-124°.

Found %: N 4.43, 4.57; S 10.18. $C_{16}H_{17}O_4NS$. Calculated %: N 4.39; S 10.39.

Benzoylacetyl (XI). a) 30.5 g of α -benzenesulfonamido- β -hydroxypropiophenone (VIa) and 300 ml of 40% sulfuric acid were boiled, with stirring, for 6 hours. The benzoylacetyl formed was steam-distilled and extracted from the distillate with benzene or ether. The extract was dried with calcium chloride, the solvent was distilled off, and the residue was distilled in vacuo. 12.8 g (86.5%) of a material was obtained with b. p. 99° (12.0 mm), n_D^{20} 1.5230; literature data [6]: b. p. 101.6-102.6° (12 mm), n_D^{20} 1.537.

The residue in the flask after steam-distillation of the benzoylacetyl was cooled, the solid product was filtered off and dissolved in 10% sodium hydroxide to separate it from the tar, and the benzenesulfonamide was precipitated with 10% hydrochloric acid. 12.8 g (81.4%) of benzenesulfonamide was obtained with m. p. 149-150°. After recrystallization from alcohol the compound melted at 155-156°, which was in agreement with the literature data [7].

b) From 31.9 g of α -benzenesulfomethylamido- β -hydroxypropiophenone (VIb) which was subjected to reaction under conditions similar to those of the preceding experiment we obtained 11.5 g (80%) of benzoylacetyl. The residue in the flask after the steam-distillation was extracted with chloroform and the chloroform was distilled off; the benzenesulfomethylamide that was separated out was distilled in vacuo. 11.7 g (68%) of a compound with b. p. 202-203° (17 mm) was obtained, which agreed with the literature data [8].

SUMMARY

It has been shown, through the examples of α -benzenesulfonamido- and α -benzenesulfomethylamido- β -hydroxypropiophenone, that the conversion of α -acylamido- β -hydroxypropiophenones to the corresponding benzoylacetyls can proceed by means of the hydrolysis of the simple nitrogen-carbon bond with splitting off of the acylamides. The formation of free amino compounds recorded by a number of investigators is not an obligatory step in the reaction and is observed only in cases where the acyl radical is sufficiently easily hydrolyzed.

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RESIN ACIDS

III. THE NATURE OF HIGH-MELTING ABIETIC ACID

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Although there has been more than a century of investigation of the nature of the resin acids, at the present time there are still many debatable aspects in this field. In particular, it has been shown only recently that α - and β -sapinic acids, which have been recognized by most of the investigators in our country as individual compounds, are not such, but are mixtures of resin acids [1, 2].

The question of the nature of "high-melting abietic acid", in our opinion, was also unclear and required additional investigation.

High-melting abietic acid has been considered an individual compound [3-7], although various physical constants have been reported for it in the literature (cf. Table 2). In this connection, each author usually assumed that the sample of the acid obtained by him was purer than those described in the literature.

Investigations on the establishment of the structural formula of this acid have been published [4], and a scheme also has been presented for the isomerization of the resin acids, explaining the formation of high-melting abietic acid [7].

The present investigation has shown that the high-melting abietic acid described in the literature is not an individual compound, but a mixture of abietic, dehydroabietic, dihydroabietic, dextro-pimaric, and other resin acids.

With regard to the scheme for the thermal isomerization of the resin acids, on the basis of the most recent investigations [1, 2, 8-12] it can be more correctly represented, in our opinion, in the following way:

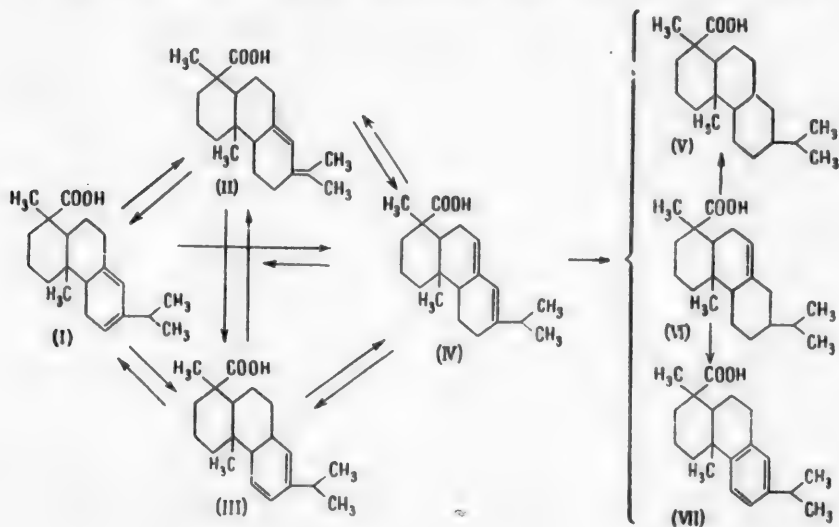


TABLE 1

Properties of Samples of High-melting Abietic Acid Prepared from Rosin

Sample No.	Wt. (in g)	Melting point	Specific rotation (in alcohol; c = 1)
1	4	190-193°	-15.1°
2	68	190-192	-13.4
3	45	190-192	-12.0
4	15	190-192.5	+ 3.5

TABLE 2

Properties of Samples of High-melting Abietic Acid (according to literature data)

Starting raw materials	Melting point	Specific rotation (in alcohol)	Literature references
Rosin	190-192°	-14.59°	[3]
Rosin	188-190	0.00	[4]
Sulfate soap	186-188	-17.36	[3]
Sulfate soap	186-188	+15.45	[6]
Low-melting abietic acid	186	+30.20	[5]

In this diagram the formulas correspond to the acids as follows: (I) levo-pimaric, (II) neoabietic, (III) palustric, (IV) abietic, (V), (VI), and (VII) tetrahydro-, dihydro-, and dehydroabietic resin acids respectively. It should be noted that all these acids (with the exception of tetrahydroabietic) have been found by us in ordinary pine resin.

EXPERIMENTAL

a) Preparation of High-Melting Abietic Acid

For the preparation of high-melting abietic acid we used pine rosin, the properties of which conformed with GOST 797-55. Its ultraviolet spectrum is shown in Fig. 1, Curve 1. We obtained from 10 kg of rosin, with exact observance of the conditions for isomerization and further purification that had been previously described [3], 4 samples of high-melting abietic acid (UV spectra of these samples are shown in Fig. 1). The properties of the samples of this acid obtained by us are given in Table 1.

For comparison, the properties of samples of high-melting abietic acid obtained by other authors are given in Table 2.

The elementary composition and the acid number of our samples of high-melting abietic acid agreed exactly with the formula $C_{20}H_{30}O_2$. The form of the crystals of the acid obtained by us was characteristic of high-melting abietic acid [3].

The data in Table 2 and Fig. 1 show that considerable variations are observed in the physical constants of the samples of high-melting abietic acid described in the literature, even when these samples were obtained from the same raw material. Such variability in the properties of high-melting abietic acid is fully understandable if we assume that this acid is a mixture of various resin acids. A change in the relative quantitative proportions of the individual components of the mixture naturally leads to a change in the physical properties of the mixture. In this case, to obtain more or less reproducible results it is necessary to observe strictly the conditions

of isomerization of the resin acids and of further crystallization of the product obtained. Krestinskii et al., [3], considered that the purest samples of high-melting abietic acid were those preparations that were levorotatory and melted at 190-192°. Therefore, for the present investigation we prepared samples of the acid with just such constants.

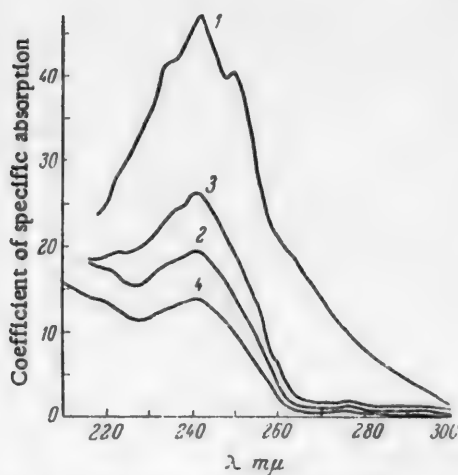


Fig. 1. Ultraviolet absorption spectra: 1) Starting rosin; 2,3,4) samples No. 1,2,4 of high-melting abietic acid (Table 1).

and $[\alpha]_D + 32.6^\circ$. After the third crystallization from acetone the salt had m. p. 142-145° and $[\alpha]_D + 46^\circ$ (UV spectrum Fig. 2, Curve 1).

After decomposition of the salt and recrystallization of the regenerated dehydroabietic acid from alcohol, it had constants characteristic of this acid [13]: m. p. 179-181.5°, $[\alpha]_D + 58^\circ$ and UV spectrum (Fig. 2, Curve 2). The elementary analysis and acid number corresponded to the composition $C_{20}H_{28}O_2$. A mixed melting point test with a known pure sample of dehydroabietic acid showed no depression. It should be noted that the UV absorption

It should be noted that the preparation of "pure" samples of high-melting abietic acid requires 8-9 crystallizations of the isomerized product, as a result of which the yield of acid becomes very small and amounts to only about 1.3% of the starting rosin.

b) Isolation of Dehydroabietic Acid from High-Melting Abietic Acid

From 65 g of high-melting abietic acid (sample no. 2) we prepared the bornylamine salt in the usual way [1]. We obtained 52 g of the salt in the crystalline form and further used it for the isolation of abietic acid (see item "c"). By evaporation of the mother liquor we obtained 27 g of crystals that also served as starting material for the isolation of dehydroabietic acid. From 27 g of crystals of the salt we obtained 17.5 g of resin acids by decomposition with acetic acid. To remove the abietic acid, the mixture was treated with 6.5 g of freshly distilled maleic anhydride in kerosene at 170-210° for 14 hours. The acids that had not reacted with the maleic anhydride were converted to the diethylamine salts (3.7 g) with m. p. 126-136°

TABLE 3

Results of Recrystallization of Bornylamine Salt of Abietic Acid

Number of recrystallizations	Material obtained (in g)	Melting point
0	52.0	133-136°
1	16.0	150-152°
2	8.0	156-158
3	4.5	162-163
4	3.2	165-166
8	0.7	169-170°*

* UV spectrum Fig. 3, Curve 1.

** UV spectrum Fig. 3, Curve 2

spectra of all the samples of high-melting abietic acid (Fig. 1, Curves 2, 3, and 4) have maxima characteristic of dehydroabietic acid at 268 and 279 mμ, which in itself indicates the presence of this acid in all the samples of high-melting abietic acid.

c) Isolation of Abietic Acid

The crystalline bornylamine salt (see item "b") was recrystallized 8 times from alcohol; the results are shown in Table 3.

As can be seen from the data of Table 3 and Fig. 3, the isolation of the acid was very difficult. The salt with m. p. 169-170° was decomposed with 0.5% acetic acid and then recrystallized twice from alcohol, as a result of which the acid was obtained with m. p. 184-186°, and $[\alpha]_D - 149.3^\circ$ (for UV spectrum see Fig. 3, Curve 3).

The elementary analysis and acid number corresponded to the composition $C_{20}H_{30}O_2$. As judged from the character of the UV spectrum, this fraction of the acids was apparently a mixture of resin acids, one of which was low-melting abietic acid and had an absorption maximum in the UV spectrum at 241 m μ . The second acid did not give a characteristic absorption band in the UV spectrum and apparently had two isolated double bonds and differed from the known resin acids in its high melting point (about 186°) and its high specific rotation (above -149°).

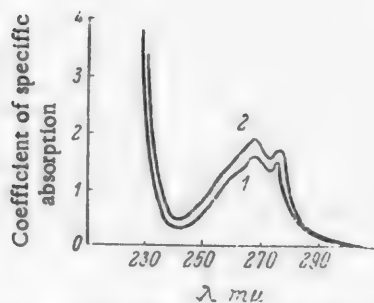


Fig. 2. Ultraviolet absorption spectra.

1) Diethylamine salts of dehydroabietic acid; 2) dehydroabietic acid.

Inasmuch as we knew that such a resin acid had not been described in the literature, a study of the nature of this acid was the subject of our further investigations.

To separate the mixture of acids mentioned, we employed crystallization of the ethanolamine, diethylamine, fenchylamine and sodium salts from various solvents, and also absorption chromatography on aluminum oxide and silica gel. However, we did not succeed in separating the mixture.

d) Isolation of Dextro-pimaric Acid

In order to remove resin acids of the type of abietic acid, 40 g of high-melting abietic acid (Sample no. 3) was heated twice with maleic anhydride (6 g) in kerosene at 200° for 20 hours. After the first treatment the acids that had not reacted with the maleic anhydride (27 g) had an m. p. 173-183° and $[\alpha]_D + 10.6^\circ$ (UV spectrum Fig. 4, Curve 1), and after the second treatment 19 g of acid was obtained with m. p. 178-183° (UV spectrum Fig. 4, Curve 2). As the UV spectra show, these acids contained a small admixture of abietic acid and a considerable amount of dehydroabietic acid. In order to further purify this fraction of the acids, it was converted to the ethanolamine salt with m. p. 146°, which after 5 recrystallizations from ethyl acetate had m. p. 160-162.5°, $[\alpha]_D + 52^\circ$, and the UV spectrum shown in Fig. 4, Curve 3. The dextro-pimaric acid regenerated from the salt had m. p. 197-200° and $[\alpha]_D + 66^\circ$ (UV spectrum Fig. 4, Curve 4). The elementary analysis and acid number of the acid corresponded to the composition $C_{20}H_{30}O_2$.

All of the data obtained above indicate that the dextro-pimaric acid isolated by us [1] actually was not pure and apparently contained an admixture of dihydroabietic acid, from which its purification was difficult [14].

e) Isolation of Dihydroabietic Acid

As is well known, the presence of dihydroabietic acid in mixtures of resin acids is demonstrated by obtaining the characteristic lactone of this acid [15, 16]. To obtain the lactone, 6.3 g of the resin acids that had not reacted with the maleic anhydride (see item "d") was treated, while being stirred, with 25 ml of concentrated sulfuric acid at -15° for 50 minutes. The mixture was poured into a beaker containing 200 ml of ice water, and the precipitate that separated out was washed and dissolved in ether. The ether solution was washed with 1% sodium hydroxide, then with water, and the ether was distilled off. After two recrystallizations from alcohol the lactone had the characteristic constants m. p. 130-131° and $[\alpha]_D - 4^\circ$ [15, 16]. A mixed melting point test of the lactone obtained with the pure lactone of dihydroabietic acid gave no depression. The pure dihydroabietic acid was prepared by us by hydrogenation of abietic acid. After purification by crystallization of its bornylamine salt, it had the constants m. p. 236-239°, $[\alpha]_D + 11.2^\circ$, and acid number 187. The elementary analysis corresponded to the composition $C_{20}H_{32}O_2$. The acid formed a lactone, in quantitative yield, with constants characteristic of it. It should be noted that dihydroabietic acid with such a high melting point was obtained for the first time [7, 13, 15-17].

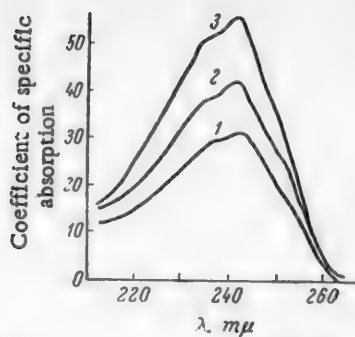


Fig. 3. Ultraviolet absorption spectra: 1) Bornylamine salts of high-melting abietic acid after first recrystallization from alcohol; 2) same after 8th recrystallization from alcohol; 3) mixture of abietic acid and acid of undetermined nature.

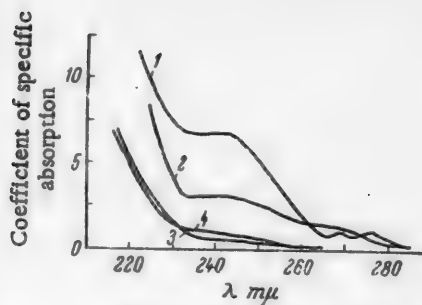


Fig. 4. Ultraviolet absorption spectra: 1) High-melting abietic acid after first treatment with maleic anhydride; 2) same after second treatment with maleic anhydride; 3) ethanolamine salt of dextro-pimaric acid; 4) dextro-pimaric acid.

SUMMARY

High-melting abietic acid is not an individual compound, but a mixture of abietic, dihydroabietic, dehydroabietic, and possibly other resin acids.

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* Original Russian pagination. See C. B. Translation.

PREPARATION OF SOME ESTERS OF ANABASINE-N-FORMIC ACID

G. V. Lazur'evskii and Yu. N. Forostyan

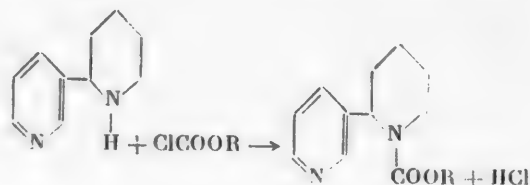
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It is known that the esters of carbamic acid (urethanes) are physiologically active. Thus, Stedman [1] established that some carbamates are highly effective insecticides. According to the data of Sekera et al., [2], esters of carbamic acid have a local anesthetic action. In isolated cases they have a systemic action – penetrating through the leaves and roots of plants, these materials are toxic to aphids and thrips [3].

In search of new compounds of this series we have prepared substituted carbamates containing an anabasine group in the molecule. Anabasine itself is similar in toxicity to nicotine [4] and is employed directly only as an insecticide. However, some of its derivatives have been recommended more than once as medicinal materials. In particular N-methylanabasine, which was first obtained by A. P. Orekhov, stimulates respiration [5]. A. S. Sadykov [6] has described a series of anabasine derivatives that are of definite interest to pharmacologists.

The demands of agriculture for anabasine sulfate at the present time have greatly decreased, since considerably more effective insecticides have been found that are prepared synthetically. However, the anabasine sulfate manufacturers are fully supplied with raw material and anabasine remains available, hence it must be considered expedient to continue the exploration of new ways of utilizing anabasine in the form of its derivatives.

We have prepared esters of anabasine-N-formic acid by a method proposed by Claisen [7], by the action of chlorocarbonic esters on anabasine in the presence of moist potassium carbonate.



For the reaction we used methyl, ethyl, propyl, and isobutyl chlorocarbonates, which in turn were prepared by a somewhat modified Rösé method [8].

The anabasine was isolated from technical anabasine sulfate and purified by conversion to the copper complex according to the directions of V. V. Udovenko [9].

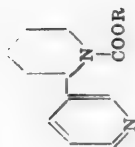
EXPERIMENTAL

Preparation of chlorocarbonic esters. Phosgene was passed into 100 ml of dry chloroform for 30 minutes. Then 50 ml of alcohol was added while the current of phosgene was continued and the mixture was strongly cooled. After this the mixture was poured into ice water and the layer of liquid that did not dissolve in the water was washed three times more with water. The chloroform solution was separated off, dried with calcium chloride, the solvent was distilled off, and the residue was fractionated.

Dry dioxane was used as the solvent for the preparation of methyl chlorocarbonate.

Methyl chlorocarbonate, b. p. 71-72°.

Esters of Anabasine-N-formic Acid



R	Yield (in %)	Boiling point (at 2 mm)	d_4^{20}	n_D^{20}	M _R	Analytical data (in %)						Hydrochloride	
						C	H	N	melting point	% Cl		found	calc
						found	calc.	found	calc.				
CH ₃	95	134-135°	1.1232	1.5345	61.01	65.27	7.47	12.56	187-188°	13.68	13.81		
C ₂ H ₅	93	146-147	1.0875	1.5223	65.71	66.34	7.36	11.73	195-196	12.95	13.09		
C ₃ H ₇	96	169-161	1.0771	1.5215	70.26	67.42	8.27	11.43	201-202	12.32	12.45		
iso-C ₄ H ₉	91	164-165	1.0536	1.5174	75.38	68.63	8.21	11.51	203-207	11.76	11.87		

22*

Ethyl chlorocarbonate, b. p. 93-94°.

Propyl chlorocarbonate, b. p. 115-116°.

Isobutyl chlorocarbonate, b. p. 128-129°.

The yield of the esters ranged from 75 to 80%.

Reaction of chlorocarbonic esters with anabasine.

In a three-necked flask fitted with a mechanical stirrer and a dropping funnel were placed 20 g ($\frac{1}{8}$ mole) of anabasine, 150 ml of ether, 17 g ($\frac{1}{8}$ mole) of potassium carbonate, and 10 ml of water. While the mixture was stirred vigorously and cooled with ice, $\frac{1}{8}$ mole of chlorocarbonic ester was added dropwise. After this the reaction mixture was left for 24 hours, with periodic stirring. Then the ether layer was decanted and the residue was treated 5 times more with ether. The ether extracts were combined and dried with calcined sodium sulfate, and the solvent was distilled off; the residue were thick brown liquids which were fractionally distilled in vacuo. The constants, yields, and analyses of the materials obtained are given in the table.

The hydrochlorides were prepared by dissolving the carbamates in absolute ether and precipitating with an ether solution of hydrogen chloride. After filtration with suction and repeated washing with absolute ether, the crystals were dried in a vacuum desiccator over solid KOH, then recrystallized from anhydrous ethanol.

SUMMARY

The methyl, ethyl, propyl, and isobutyl esters of anabasine-N-formic acid were prepared by the reaction of anabasine with chlorocarbonic esters and were characterized. The preparations were submitted for pharmacological testing.

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INVESTIGATION OF THE REACTION OF LUPININE WITH PHOSGENE

G. V. Lazur'evskii and Yu. N. Forostyan

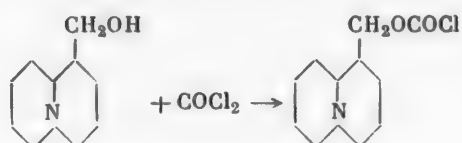
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As was pointed out in the preceding communication,* some urethane derivatives have interesting physiological activities. Shriner and Hickey [1] reacted chlorocarbonic esters with 1-diethylamino-3-aminopropane to prepare several urethanes having an anesthetic effect. A. P. Terent'ev and A. N. Kost [2] considerably expanded this series of carbamates.

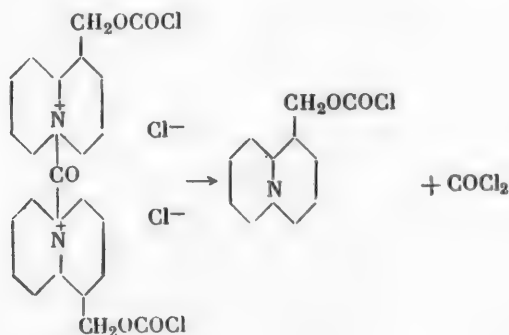
Having in view the availability of lupinine, which is present in technical anabasine sulfate, we set up the problem of preparing its chlorocarbonate and the corresponding urethanes.

From the work of A. Panashchenko [3] it is known that the alkaloid lupinine does not have a strong effect on animal and human organisms, but on reaction with other compounds containing active functional groups it may yield very interesting medicinal materials. Thus, M. M. Katsnel'son and M. I. Kabachnik [4] synthesized, among other lupinine derivatives, a new anesthetic — the p-aminobenzoic acid ester (lupicaine).

To obtain the lupinine ester of chlorocarbonic acid we employed the method of R6se [5], i. e., we reacted an excess of phosgene with lupinine and washed the reaction product with ice water.

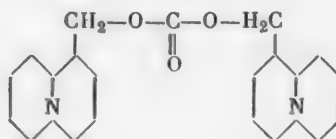


However, in the case of lupinine the yield of the final product proved to be low. Apparently the presence of a tertiary nitrogen in lupinine hindered the course of the main reaction. Evidently a part of the phosgene was expended in the formation of the salt, which like the pyridine salt [6] easily decomposes in water and forms urea and diphenylurea with ammonia and aniline.



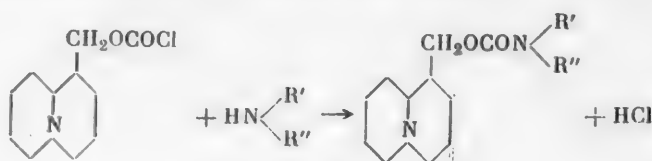
* Cf. J. Gen. Chem. 29, 3498 (1959). Original Russian Pagination. See C. B. translation.

When the reaction is carried out with insufficient phosgene, not the ester, but the salt is formed initially, since only lupinine and phosgene* can be found in the products of decomposition by water.* If sodium lupinate, obtained directly in separating anabasine and lupinine [7], is used instead of lupinine, then the yield of the ester can be considerably increased.



The lupinine ester of chlorocarbonic acid is completely stable in water; on prolonged heating in toluene it yields the dilupinine ester of carbonic acid.

By the action of lupinine chlorocarbonate on ammonia, dimethylamine, and 1-dimethylamino-3-amino-propane the corresponding urethanes of lupinine were obtained, the properties of which are given in the table.



EXPERIMENTAL

Reaction of lupinine with phosgene. In a three-necked flask fitted with a stirrer and dropping funnel was placed 100 ml of a 20% benzene solution of phosgene. While the solution was cooled and stirred, 10 g of phosgene lupinine dissolved in 100 ml of dry benzene was introduced, and a vigorous stream of phosgene was passed through. After addition of all the lupinine, passage of the phosgene was stopped; a thick, viscous mass was formed on the bottom of the reaction vessel. The excess COCl_2 was removed by blowing dry nitrogen through. The solvent was poured off and the residue was placed in a vacuum desiccator over KOH. A crystalline product could not be obtained even on prolonged standing. The reaction mixture was insoluble in the usual organic solvents. When it was shaken with water, copious evolution of phosgene was observed (test for anabasine or aniline). In the lower part of the separatory funnel in this process an oily liquid collected, which was separated off and distilled in vacuo. The yield of lupinine chlorocarbonate was 7.3 g (53%).

B. p. 75-76° at 1 mm, d_4^{20} 1.1665, n_D^{20} 1.5085, M_R 59.20, calc. 59.43.

Found %: C 56.75; H 7.59; N 6.38; Cl 15.18. $\text{C}_{11}\text{H}_{18}\text{O}_2\text{NCl}$. Calculated %: C 57.02; H 7.83; N 6.04; Cl 15.30.

The methiodide formed colorless needles with m. p. 246-247° (from methanol).

The aqueous portion was extracted 5 times with ether; the extracts were combined and dried with calcined sodium sulfate. After the ether was distilled off, lupinine was obtained in crystalline form (1.5 g).

When the reaction was carried out with sodium lupinate in toluene solution, the yield of lupinine chlorocarbonate was 84%.

Preparation of dilupinyl carbonate. The intermediate product obtained by the reaction of phosgene with lupinine (an oil insoluble in organic solvents) foamed greatly when we attempted to distill it in vacuo. When this product was heated for a long time in boiling solvent (benzene, toluene), dilupinyl carbonate was formed. The excess phosgene and the solvent were distilled off and the residue was treated with sodium carbonate and shaken with ether. After the ether layer had been washed with water, the ether was dried and distilled off. Some lupinyl chlorocarbonate was isolated by fractionation in vacuo. The main part of the material distilled at 206-207° (yield 74%).

* The presence of phosgene can be determined conveniently with filter paper moistened with anabasine. In the presence of phosgene an intense red color is produced.



Urethanes of Lupinine	R'	R''	Yield (in %)	Boiling point (at 1 mm)	d_4^{20}	n_D^{20}	Analytical Data (in %)			
							MRD		C	
							found	calc.	found	calc.
							found	calc.	found	calc.
Lupinylurethane	H	H	57	116—117°	1.0906	1.5037	57.32	57.54	67.05	62.23
Dimethylupinylurethane	CH ₃	CH ₃	64	123—124	1.0489	1.4974	67.10	67.37	64.69	64.97
N-(1-Dimethylamino-3-propyl)-lupinylurethane	H	(CH ₂) ₃ N(C ₂ H ₅) ₂	52	136—137	1.9119	1.4412	94.31	94.06	66.27	66.42

d_4^{20} 1.0848, n_D^{20} 1.5165, MR_D 101.21; calc. 101.55.

Found %: C 69.37; H 9.72; N 7.74. $C_{21}H_{36}O_3N_2$.
Calculated %: C 69.19; H 9.96; N 7.68.

Dipicrate, m. p. 157–159° (from acetone and ethanol 1 : 1).

Dimethiodide, m. p. 233–234° (from methanol).

Reaction of equivalent amounts of lupinine and phosgene. 32 g of lupinine was dissolved in 200 ml of dry toluene and this solution was added in portions, with cooling and stirring, to 100 ml of a 10% toluene solution of $COCl_2$. After the mixture had stood for 24 hours, dry nitrogen was passed through it for 30 minutes, the toluene was removed by decantation, and the viscous residue that had formed on the bottom of the flask was treated in the following manner.

Half of the product was dissolved in 100 ml of dry toluene and a current of ammonia was passed through it, whereupon we observed the formation of urea (2.5 g) and ammonium chloride (5 g), which were filtered off after the separation of precipitate ceased and were separated by repeated washing with anhydrous alcohol. The residue that had crystallized after the toluene was distilled off under vacuum from a water pump was lupinine with m. p. 68–69°.

To the other portion of the product was added 100 ml of ice water, and the base was extracted with ether. After appropriate treatment of the extract, the starting lupinine was isolated with m. p. 68–69°.

Preparation of lupinylurethane. 100 ml of absolute ether was saturated with ammonia and 5 g of lupinine chlorocarbonate in 50 ml of ether was added. After this, NH_3 was passed through the mixture for 6 hours. The ammonium chloride that precipitated was separated off by filtration, the solvent was distilled off, and the residue was fractionated in vacuo. (Properties and analysis of urethanes are given in the table).

Hydrochloride, m. p. 210–211° (from anhydrous alcohol).

Preparation of dimethylupinylurethane. 100 ml of dry benzene was placed in the reaction flask, previously prepared dimethylamine was passed through it for 30 minutes, then 7 g of pulverized KOH was added and (without stopping the stream of dimethylamine) 15 g of lupinine chlorocarbonate was introduced. After addition of all the chlorocarbonate the reaction flask

was heated on a water bath for 6 hours while dimethylamine was continuously passed through. After this, the benzene and excess dimethylamine were distilled off under the vacuum from a water pump. The residue was dissolved in dilute alkali, the base was extracted with ether, the ether extracts were dried with fused potassium carbonate, and after the solvent was distilled off, the residue was fractionated in vacuo.

Methiodide, m. p. 176-177° (from methanol).

Preparation of N-(1-diethylamino-3-propyl) lupinylurethane. 1-Diethylamino-3-aminopropane was prepared by a method described by A. P. Terent'ev and A. N. Kost [8].

5 g of 1-diethylamino-3-aminopropane in 50 ml of toluene and 1.5 g of finely ground KOH were placed in a flask and then 8 g of lupinine chlorocarbonate was added. The reaction mixture was heated for 12 hours on an oil bath. After this the KCl was filtered off along with the excess KOH. The filtrate was collected and the toluene was distilled off from it under vacuum from a water pump and the residue was treated as in the preceding experiment.

Methiodide, m. p. 215-217° (from ethanol and methanol 1 : 2).

SUMMARY

1. It has been shown that when phosgene and lupinine react, the dlupinine salt of phosgene is formed.
2. Lupinine chlorocarbonate and dilupinine carbonate have been prepared and characterized.
3. Lupinylurethane and N-(1-diethylamino-3-propyl) lupinylurethane have been synthesized from lupinine chlorocarbonate.

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INVESTIGATION OF THE CHEMICAL STRUCTURE OF THE ANTIBIOTIC HELIOMYCIN

I. SOME DATA ON THE CHEMICAL NATURE OF HELIOMYCIN

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Heliomycin, one of the few known antibiotics having antiviral activity, was isolated by M. G. Brazhnikova et al., [1] from the mycelium of a ray fungus belonging to the species Actinomyces flavochromogenes (var. heliomycini).

The present article reports preliminary experimental data on the chemical nature of the antibiotic.

Heliomycin is a yellow material that crystallizes relatively readily from dioxane or a mixture of acetone and methyl ethyl ketone as orange-yellow needles with m. p. 315-325° (decomp.). The material not only is colored, but is a dye with an affinity for animal fibers: It dyes wool without a mordant to a yellow color, and with a mordant to a brown, and in aqueous solutions of alkalis it gives an intense dark red color. Furthermore, heliomycin shows the phenomenon of halochromism, forming a red color with concentrated hydrochloric acid and a green with sulfuric. With an aqueous solution of ferric chloride in the presence of alcohol it displays a phenolic character (cherry red coloration). Crystals of the antibiotic in most cases contain molecules of the solvent employed. With metals it forms brightly colored complexes. Thus, for example, heliomycin and nickel give a bright red compound that crystallized from organic solvents and contains 1 atom of nickel to 2 molecules of heliomycin. Heliomycin does not form hydrazones with phenylhydrazine or 2,4-dinitrophenylhydrazine, giving with the first of these an orange-colored molecular compound that breaks down on crystallization into the starting products. The antibiotic under investigation undergoes azo coupling with diazonium salts. Thus, a brown monoazo product was obtained by coupling with p-nitrophenyldiazonium salts.

As regards the chemical character of heliomycin, it is an acid, apparently stronger than the aromatic phenols. By potentiometric titration of water-acetone solutions a pK value of 5.8-5.9 was found.

In the course of the investigation of the antibiotic several derivatives of it were prepared. Heliomycin was methylated by diazomethane in dioxane solution, forming a product with m. p. 260-290° (decomp.); however, when it was methylated with dimethyl sulfate in alkaline solution, a methylation product could not be obtained. Heliomycin can be acetylated with acetic anhydride to yield products of various degrees of acetylation, depending on the conditions. When the acetylation was carried out with an excess of acetic anhydride at 100°, a product (I) was formed with m. p. 265-267°, but when the acetylation was carried out under the same conditions with the addition of dry pyridine, a product (II) was obtained with m. p. 238-239°. Acetylation product (I) contained one acetyl group, and product (II) contained two. Product (I) could be converted to (II) by further acetylation, and (II) was converted to (I) by careful partial deacetylation.

On the basis of the data available, we can assume an approximate empirical formula $C_{19}H_{14-16}O_5$ or $C_{25}H_{18-20}O_6$ for heliomycin, which can be defined more accurately only after the investigation of a number of derivatives and cleavage and hydrolysis products of heliomycin.

To elucidate the question of the presence of oxygen-containing rings in the antibiotic molecule, we carried out experiments on its alkaline hydrolysis. It was found that both under conditions of alkaline hydrolysis

with 2 N NaOH and on fusion with solid KOH at 270-290° there was no change observed in the antibiotic. Analytical data and complete correspondence of the IR absorption spectrum (Fig. 1) showed the identity of the material formed on acidification of the alkaline hydrolyzate with the starting heliomycin. The latter was also

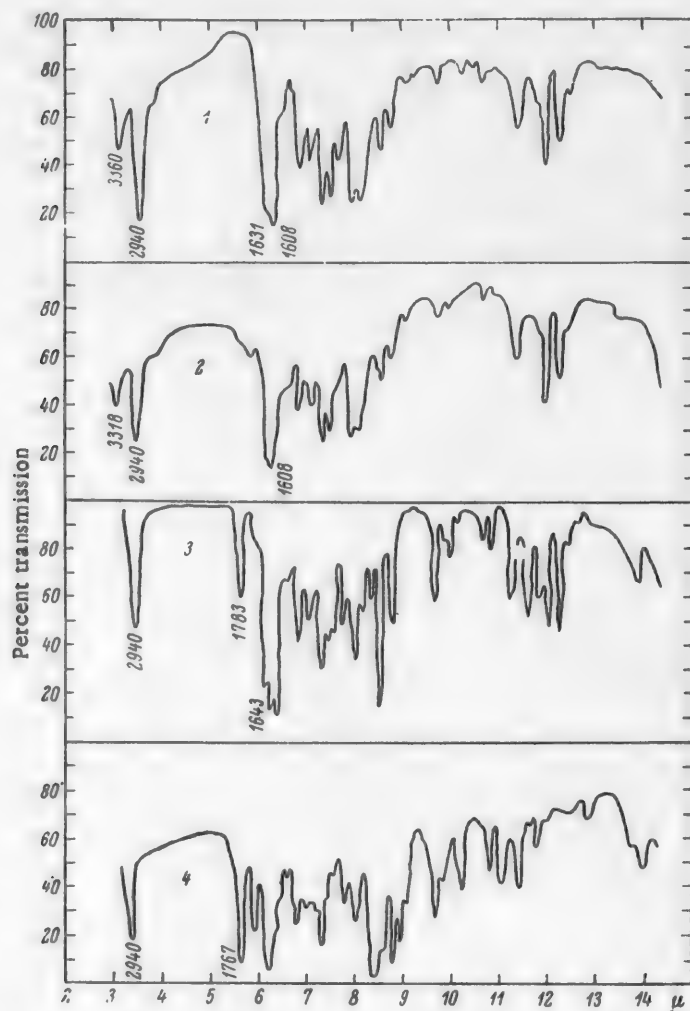


Fig. 1. Infrared absorption spectra: 1) Heliomycin; 2) heliomycin that has been subjected to alkaline hydrolysis; 3) acetyl derivative (I) of heliomycin; 4) acetyl derivative (II) of heliomycin.

confirmed by acetylation of the product of alkaline hydrolysis with acetic anhydride, which led to the formation of an acetyl derivative coinciding in its properties with acetyl derivative (I) obtained from pure heliomycin.

For microdistillation with zinc dust we employed acetylation product (II) with m. p. 238-239° and obtained a yellow, partially crystallizing oil. Benzene solutions of the product of distillation had a strong blue fluorescence. After removal of the solvent a crystalline mass remained with a typical aromatic odor, predominantly like that of naphthalene; the substances yielded a picrate in the form of a brown powder with m. p. 122-123°. (It is known that compounds of the tropolone group, for example purpurogallin, also form substances of the naphthalene series on distillation with zinc dust [2, 3]).

The results of the chemical investigation of heliomycin (data from the experiments on distillation of heliomycin with zinc dust, reaction with ferric chloride, coupling with diazonium salts, inertness of the carbonyl group,

comparatively high acid dissociation constant, formation of compounds with metals, and other properties) indicate some similarity of this antibiotic with the tropolone compounds [4].

The IR and UV absorption spectra of the antibiotic itself and of some of its derivatives also were studied.

The IR absorption spectra were obtained with an IKS-11 instrument with a NaCl prism in the region 2.15-14 μ , using a suspension of the crystalline materials in vaseline oil. In the absorption spectrum of heliomycin

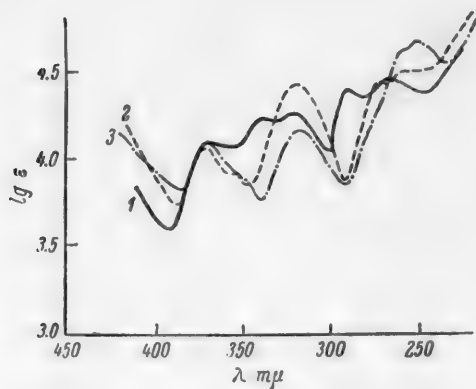


Fig. 2. Ultraviolet absorption spectra: 1) Heliomycin; 2) acetyl derivative (I) of heliomycin; 3) acetyl derivative (II) of heliomycin.

(Fig. 1, Curve 1) attention is drawn to the absorption band at 1631-1608 cm^{-1} , which lies in the region of the absorption of $>C=C<$ double bonds. However, the very great intensity of this somewhat bifurcated band permits the conclusion that it is due to the carbonyl group. Absorption bands for carbonyl groups of such low frequency can be observed only under conditions of strong conjugation of the bond of the $C=O$ group with aromatic systems and where it participates in the formation of very stable hydrogen bonds (bonds of the clathrate type). Absorption bands of this type are observed, for example, in the spectra of β -hydroxyketones (1625 cm^{-1}), hydroxyquinones (1622-1630 cm^{-1}) and tropolones (1612-1620 cm^{-1}) [5-8]. It also should be noted that the band corresponding to the carbonyl group of heliomycin is rather broad; this fact possibly is due to the presence in the molecule of the antibiotic of other carbonyl groups. Furthermore, the position of the absorption band for the hydroxyl group at 3360 cm^{-1} differs considerably from the frequencies 2600-2700 cm^{-1} usually characterizing hydroxyl groups that participate in clathrate type hydrogen bonds. In the region 3100-3200 cm^{-1} absorption bands frequently are found for the hydroxyl of tropolone compounds [9]. Thus, the peculiarities and the character of the distribution of the absorption bands of the carbonyls (1608-1631 cm^{-1}) and the hydroxyl group (3360 cm^{-1}) indicate some similarity between the IR spectra of heliomycin and the tropolones.

In the IR absorption spectrum of the monoacetyl product (I) (Fig. 1, Curve 3) we observe the disappearance of the absorption band corresponding to the hydroxyl group (3360 cm^{-1}) and the presence of an absorption band at 1783 cm^{-1} that is in the region of the band for anhydrides or γ -lactones [5]. However, relation of this band to an acetyl group connected through an oxygen with an unsaturated system of the type $>C=C-O-COCH_3$ would be more probable.

According to the investigations of L. Bellamy and E. Hartwell [5, 10], the presence of a conjugated system of bonds or even of one double bond on the carbon of an ester group leads to an increase in the frequency of the absorption of the carbonyl group to 1770-1780 cm^{-1} . From this it follows that the hydroxyl in heliomycin has a phenolic or vinyl character, and it is completely possible that this also is a hydroxyl of a tropolone nucleus. Inasmuch as the IR absorption spectrum of the monoacetyl product (Fig. 1, Curve 3) does not have bands corresponding to hydroxyl groups, substance (I) does not contain hydroxyls; however, it can be acetylated to form the diacetyl derivative (II). Since the IR absorption spectrum of the diacetyl derivative (II) (Fig. 1, Curve 4) does not show the absorption band for an acetyl carbonyl corresponding to the usual saturated ester (1730-1740 cm^{-1}), but the band at 1783 cm^{-1} is only considerably increased in intensity, it can be assumed that the second acetylation leads to the appearance of the grouping $>C=C-O-COCH_3$.

It remains to be assumed that on further acetylation of the acetyl derivative (I) with the formation of the product (II), enolization of the carbonyl group in the molecule takes place and as a result of this a vinyl-ester grouping is formed.

We obtained the UV absorption spectra of the compounds under investigation with a SF-4 spectrophotometer in dioxane and alcohol solutions at concentrations of 10^{-4} M. On looking at the UV absorption spectra for heliomycin and its acetyl derivatives (I) and (II) (Fig. 2), there are two clearly visible characteristic regions of absorption within the range 250-290 and 320-370 $m\mu$. According to the data in the literature [4], tropolones and tropolones give intense absorption bands in the ultraviolet in the range 225-270 and 280-400 $m\mu$.

When the UV absorption spectrum of the hydrocarbon obtained on distillation of heliomycin with zinc dust is compared with the absorption spectra of naphthacene, phenanthrene, anthracene, and their homologs, a distinct difference is observed. Some similarity is observed in the ultraviolet absorption spectra of the hydrocarbon under investigation and that of α -benzyl-naphthalene (Fig. 3) [11].

The results of the preliminary chemical and physicochemical investigation of the antibiotic indicate the expediency of a detailed study of the question of the presence in heliomycin of a benzotropolone system.

EXPERIMENTAL

In our work we used heliomycin purified by repeated recrystallization from dioxane or a mixture of methyl ethyl ketone and acetone (1 : 1) and carefully dried in a vacuum desiccator at 80-90°.

For (a): Found %: C 70.60, 70.79; H 4.38, 4.52. H_{act} number (by Tserevitinov method): 4.75, 522; for (b): 5.70, 6.23. M 385 (by Rast method). $C_{19}H_{15}O_5$. a). Calculated %: C 70.36; H 4.98. H_{act} number 5.0 M 324. $C_{23}H_{19}O_6$. b) Calculated %: C 70.76; H 4.56. H_{act} number 6.0 M 389.

Coupling of heliomycin with p-nitrophenyldiazonium. 0.1 g of heliomycin was dissolved in 40 ml of acetone with the addition of 2 drops of 10% aqueous NaOH solution. To the solution was added, with stirring, 0.5 ml of a solution of p-nitrophenyldiazonium chloride and the mixture was stirred for 20 minutes, after which a saturated solution of sodium acetate and 0.1 N hydrochloric acid solution were added until there was a weak acid reaction to Congo. Then the reaction mixture was diluted with 50 ml of water and left to stand for 1 hour, after which the precipitate was filtered off and carefully washed with water, dried slightly, and recrystallized from glacial acetic acid. 0.07 g (51%) of a brown, crystalline material was obtained.

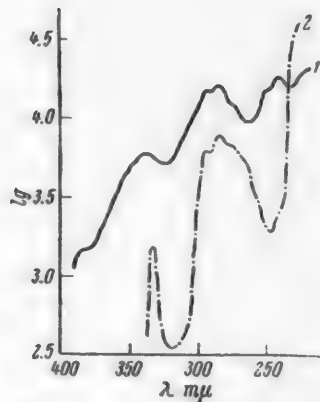


Fig. 3. Ultraviolet absorption spectra: 1) Hydrocarbon obtained after distillation of heliomycin with zinc dust; 2) benzyl-naphthalene.

Found %: N 7.96, 7.64. $C_{29}H_{19}O_5N_3$. Calculated %: N 7.82.

Acetylation of heliomycin. a) Preparation of acetylation product (I). 0.2 g of heliomycin and 2.0 g of acetic anhydride were heated for 3 hours at 100°. The reaction mixture was left overnight, then the precipitate that had crystallized was filtered off and recrystallized from anisole. The purified product was dark yellow in color, melted at 265-267°, and was poorly soluble in water, alcohol, benzene, and other organic solvents. Yield 0.15 g (75%).

Found %: C 68.38, 68.37; H 4.54, 4.38. H_{act} number 3.85, 4.27. $C_{21}H_{18}O_6$. Calculated %: C 69.02; H 4.69. H_{act} number 4.0.

b) Preparation of acetylation product (II). 0.2 g of heliomycin, 1.95 g of acetic anhydride, and 0.05 g of dry pyridine were heated at 100° for 3 hours. After standing for an additional 24 hours at room temperature, the precipitate was filtered off, washed on the filter with ether, and purified by recrystallization from isoamyl alcohol. The product was a bright yellow crystalline powder melting at 238-239°. Yield 0.12 g (55%).

Found %: C 67.62, 67.34; H 4.71, 4.37. H_{act} number 2.52. $C_{23}H_{20}O_7$. Calculated %: C 67.80; H 4.70. H_{act} number 3.0.

Hydrolysis of acetyl derivative (II) with 20% sulfuric acid. 0.1 g of acetyl derivative (II) and 8.0 ml of 20% sulfuric acid were boiled at 150-160° for 3 hours. After the reaction mixture was cooled, the precipitate was filtered off, washed with water, and recrystallized from anisole. Yield 0.07 g. M. p. 265-267°. The material obtained did not give a depression in melting point with acetyl derivative (I) of heliomycin.

Methylation of heliomycin with diazomethane. To a suspension of 0.2 g of heliomycin in 60 ml of dioxane was added, with vigorous stirring, 25 ml of a dioxane solution of diazomethane prepared from 2.0 g of nitroso-methylurea. In 15-20 minutes the heliomycin dissolved and a finely crystalline precipitate began to separate from the reaction mixture. Stirring was continued for 3.5 hours, after which the precipitate product was filtered off. Yield 0.09 g. The material obtained was poorly soluble in dioxane, glacial acetic acid, and isoamyl alcohol, and moderately so in anisole. After recrystallization from anisole the product melted at 260-290° (decomp.).

Found %: C 70.77; H 5.22. $C_{20}H_{18}O_5$. Calculated %: C 70.99; H 5.36.

Alkaline hydrolysis of heliomycin. 1.13 g of heliomycin was dissolved in 25 ml of 2 N NaOH and the solution was poured into a flask fitted with a reflux condenser and was heated at 120-140° in a stream of nitrogen for 4 hours. Then 35 ml of 2 N hydrochloric acid was added to the dark red alkaline solution; the solution became yellow and a copious precipitate separated out. The precipitate was filtered off, washed with water, and dried in a vacuum desiccator. The weight of the precipitate was 1.03 g, m. p. 313-323° (decomp.). A mixed sample with pure heliomycin gave no depression in melting point.

Alkaline fusion of heliomycin with chemically pure potassium hydroxide yielded a yellow product with m. p. 314-318°, which was identical in properties and elementary analysis with the starting heliomycin.

Distillation of acetyl derivative (II) with zinc dust. Acetyl derivative (II) (in 8-10-mg portions) was mixed with 20 times the amount of zinc dust that had previously been washed with 3% hydrochloric acid and carefully dried. Each portion of the mixture was placed in a tube 20 cm long and with an internal diameter of 6 mm, one end of which was sealed and drawn out into a capillary. The contents of the tube were heated quickly in an open flame and a light yellow oil was distilled into the cold part of the tube. At the end of the distillation the tube was cut open and the oil was washed out with benzene. 0.21 g of the acetyl derivative of heliomycin in all was subjected to distillation. The benzene solution obtained by washing out all of the tubes showed a blue fluorescence; after removal of the benzene a dark yellow oil was obtained that crystallized partially and had a strong naphthalene odor. In view of the small amount of this oil, we were not able to isolate and identify the hydrocarbon. We obtained a picrate from the oil, which after being washed with water (to remove picric acid) and crystallized from alcohol formed a brown powder with m. p. 122-123°. A mixed sample with picric acid melted at 114-116°.

SUMMARY

1. Some chemical characteristics of the antibiotic heliomycin and a number of its derivatives have been studied.
2. The IR and UV absorption spectra of heliomycin and its acetyl derivatives have been investigated.

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LETTERS TO THE EDITOR

COMMENT IN CONNECTION WITH THE ARTICLE

BY D. JERCHEL AND L. JAKOB ENTITLED

"N-PYRIDYLAMINOPHENOLS FROM PYRIDYL AMINOPHENOL ETHERS;
A NEW REARRANGEMENT"

A. F. Vompe, N. V. Monich, and N. F. Turitsyna

In a recently published article [1] D. Jerchel and L. Jakob noted that the reaction of γ -phenoxy pyridine with ammonia leading to the formation of γ -aminopyridine [1], which was investigated by D. Jerchel et al., was under further development as a method of preparing 4-substituted pyridines with aliphatic and aromatic amine groups. The German authors made reference in this connection both to their own paper [4] and to our work in the journal *Tetrahedron* [4].

In this connection we consider it necessary to state that in the method developed by us for the synthesis of γ -amino-substituted pyridines we started not with the reaction of D. Jerchel and his co-workers, but with our own investigations on the cyclization of the salts of dianils of β -phenoxy-substituted glutamic aldehydes. This follows with complete clarity from our paper [4], which is cited by the German authors (Cf. also [5]).

Thus, the statement of D. Jerchel and L. Jakob is based on an obvious misunderstanding. We also wish to note that the method of synthesis of γ -amino-substituted pyridines was published by us [5] approximately a year before the appearance of the similar paper by D. Jerchel and L. Jakob.

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RESEARCH BY SOVIET EXPERTS

Translated by Western Scientists

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